"TARGET ORGAN DAMAGE AMONG NEWLY DIAGNOSED RURAL ESSENTIAL HYPERTENSIVES"

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CHENNAI – TAMILNADU

CERTIFICATE

This is to certify that this dissertation entitled **"TARGET ORGAN DAMAGE AMONG NEWLY DIAGNOSED RURAL ESSENTIAL HYPERTENSIVES"** submitted by **Dr.D.BABU VINISH** to The Tamil Nadu Dr.M.G.R. Medical University, Chennai is in partial fulfillment of the requirement for the award of M.D. degree Branch I (General Medicine) and is a bonafide research work carried out by him under direct supervision and guidance.

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DECLARATION

I **Dr. D.Babu Vinish** declare that I carried out this work on **"TARGET ORGAN DAMAGE AMONG NEWLY DIAGNOSED RURAL ESSENTIAL HYPERTENSIVES"** at Department of General Medicine, Government Rajaji Hospital during the period of January 2005 – December 2005. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any university, board either in India or abroad.

This is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulation for the M.D. Degree examination in General Medicine.

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ABBREVIATIONS

Hypertension	-	Essential Hypertension
BP	-	Blood pressure
DBP	-	Diastolic Blood pressure
DT	-	Deceleration Time
GBM	-	Glomerular Basement Membrane
gms	-	Grams
IVRT	-	Intra Ventricular Relaxation Time
LNE	-	Lymphnode Enlargement
LV	-	Left Ventricle
MAP	-	Mean Arterial Pressure
RAS	-	Renin Angiotensin System
SBP	-	Systolic Blood Pressure
SD	-	Standard Deviation
TOD	-	Target Organ Damage

CONTENTS

INTRODUCTION

Hypertension is widespread in the community and is the major contributing factor for cardiovascular morbidity and mortality. To add to this it also shows its evil paw to nearly every organ in the body.

History

Target organ damage and hypertension has been dealt by western authors as early as 1800's and vast review of literature has been published in the west. In sharp contrast blood pressure and target organ damage had been dealt by Charaka even before the birth of Christ when he had given Raulfina Serpitina for his patients who suffered from hypertension, but we still lack good literature of the prevalence and the impact of target organ damage in newly detected hypertensives to our dear society.

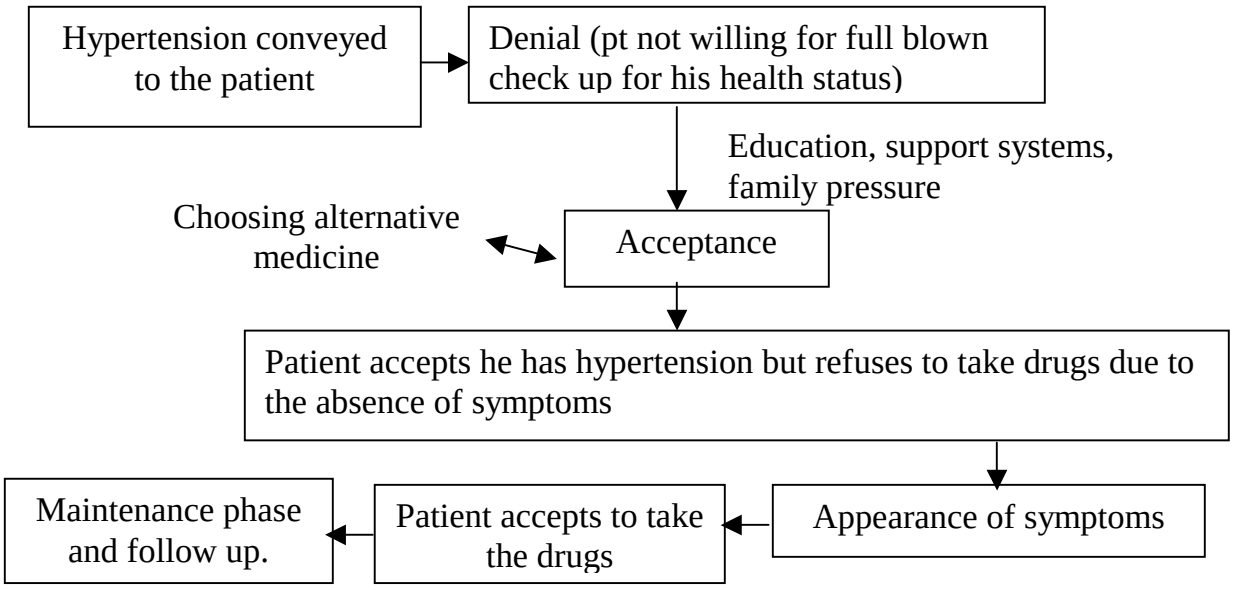
Euro American views of target organ damage in hypertension

The Joint National Committee (JNC)[1] VII states that not to search for target organ damage as an essential procedure in the diagnostic approach of the high blood pressure state, but the European guidelines given by the European Society of hypertension[2] suggests that searching for target organ damage is of

crucial importance for stratifying the cardiovascular risk of the hypertensive population.

Indian population and hypertension

The Indian population is not well informed about health and illness. When a patient comes to the hospital for some other complaint and is diagnosed to have hypertension, the first response by the patient is to deny. The various stages involved in the treatment of hypertension is furnished below:



Hypothesis / Assumptions

Most of the Indian patients come to a doctor of modern medicine only when the symptoms are likely to cause him distress in his routine activities or if these symptoms did not improve by other systems of medicine. So, there is a higher probability that our patient would have target organ damage at

presentation. Moreover there are no published reports available on covert target organ damage in newly detected hypertensive population and their possible association, so this study was undertaken.

AIMS

1. To find out the prevalence of Target organ damage in non alcoholic, non smoker, non obese, non dyslipidemic, newly detected rural essential hypertensives.

2. To identify the pattern of Target organ damage.

3. To analyse the gender difference.

4. To assess the interrelationship between Target organ damage.

REVIEW OF LITERATURE

HISTORY

Introduction

Blood pressure was measured for the first time by Stephen Hales in 1773 along with which he described the importance of blood volume in blood pressure regulation[3].

Sphygmomanometer and blood pressure recording

Riva Rocci in1896 had invented the inflatable cuff sphygmomanometer that we use even today for the measurement of brachial systolic pressure; while Korotkoff in 1904 described the auscultatory method along with Korotkoff sounds to find out the diastolic pressure[4].

Pathogenesis

While going into the pathogenesis the contribution of the peripheral arterioles in maintaining the blood pressure was described by Lower in 1669 and subsequently by Senae in 1783.

The role of vasomotor nerves in hypertension was represented in a monograph by William Dayliss in 1923[3].

Target organ damage and Hypertension

Sir William Cull and H.G. Sutton (1872) described the cardiovascular changes in hypertension. Richard Bright in the first half of the 19th century observed the changes of hypertension on the cardiovascular system in chronic renal failure.

Irwin, Page, Gold Blatt in the later 19th century worked extensively on the biochemical basis of hypertension from which we have derived our concepts of systemic hypertension[3].

Gower in 1870 was the first person who described arteriolar vasoconstriction in the retina in cases of elevated blood pressure using an ophthalmoscope[4].

Others

Fredrick Mahamood was the one who incorporated blood pressure measurement as a part of clinical evaluation[3].

Frank in 1911 suggested the term essential hypertension in patients in whom no obvious cause of hypertension could be found out[4].

Table 1: Historical events in hypertension in chronological order

Year	Event
1669	Contribution of peripheral arterioles in maintaining blood pressure – by Lower.
1773	Blood pressure was measured for the first time by Stephen Hales
1870	Ocular changes in hypertension by Gower
1872	Cardiovascular changes in hypertension by Sir William Cull and H.G. Sutton
1896	Riva Rocci invented the inflatable cuff sphygmomanometer
1904	Korotkoff described the ausculatatory sounds – measurement of diastolic blood pressure
1911	The term essential hypertension coined by Frank
1923	The role of vasomotor nerves in hypertension represented in a monograph by William Dayliss

First half 19th century	Hypertension and CVS in patients with CRF Richard Bright
Late 19th century	Biochemical work on hypertension by Gold Blatt Irwin, Page, Van Slyke.

Prevalence

The prevalence of hypertension depends on both racial composition and the criteria used to define the condition and the varying prevalence may be due to the various cutoff values used. For an example.

- Bechgard 1946[5] suggested a value of 160/100 mmHg
- While Perala 1948 suggested a value of 140/90 mmHg
- And Evans 1956 suggested 180/110 as a cutoff value for demarcating normotension from hypertension.
- The Joint National Committee[1] was formed in the United States to define hypertension, review it and to give new criteria and guidelines for treatment as newer advances occurred in the field. Most of the people in the world follow the JNC VII guidelines which was circulated in 2003. Europe follows its own guidelines as suggested by European society of Hypertension.

In the Framingham study in a sub-urban population almost one half had hypertension as the pressures were greater than 140/90.

The National heath and nutrition examination surveys in the US reported that the prevalence of hypertension was about 20% in the US population in 1991[6].

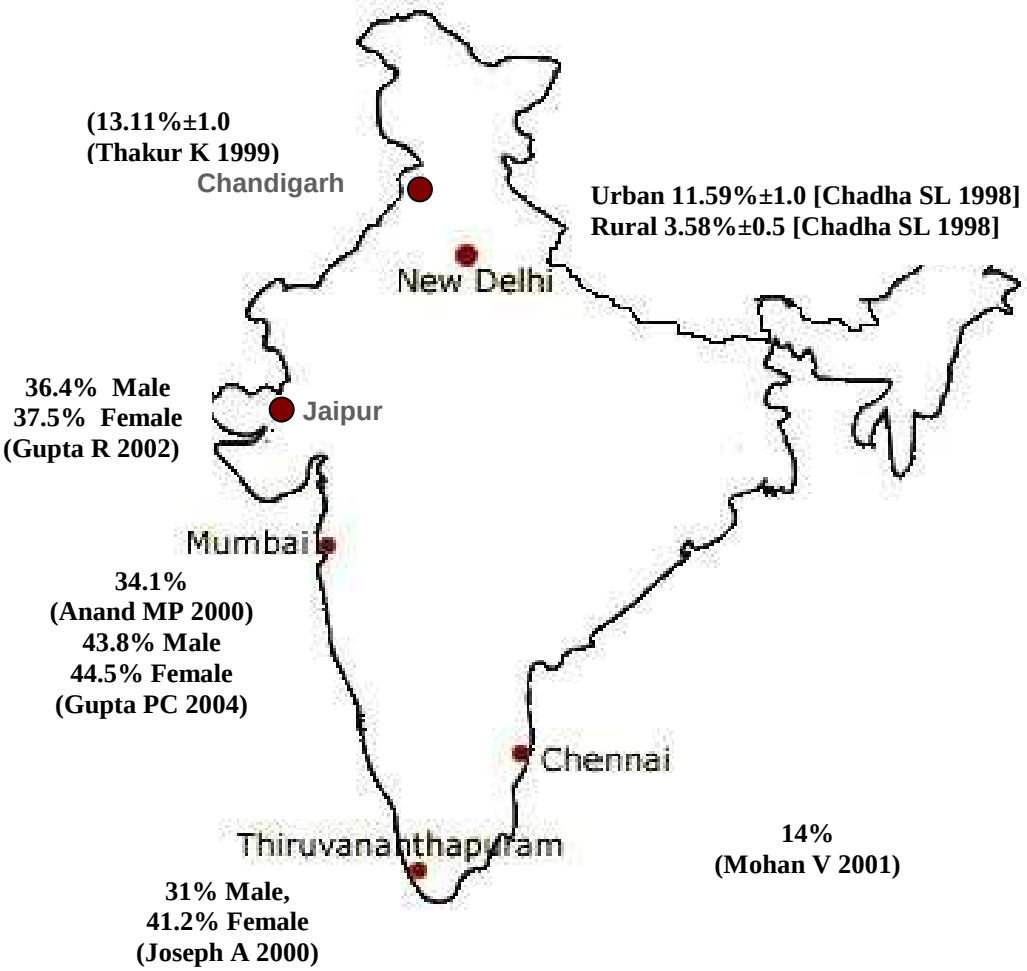
In India, no specific data are available on the prevalence of hypertension nation wide. Researches carried out in the mid 1950's reported a prevalence of 1.2 to 4%, but studies in the late 1980's and 1990's showed variation in the prevalence from 1 to 15%.

The prevalence of hypertension in the metropolitan of Chennai and Mumbai has reached about 30 to 40%[7,8].

A pooling of epidemiological studies shows hypertension is present in 25% of urban and 10% rural population in India[9].

It is estimated that the approximate number of persons affected by hypertension in India is 19,57,85,036[10] in an estimated population of 106,50,70,607[11].

Fig. 1 Prevalence of hypertension in India over the years 1998-2004*



*** Source:** Gupta R: Trends in Hypertension epidemiology in India: J Hum Hypertens 2004: 18; 73-78.

Definition[12]

Blood pressure in a population would be a typical bell shaped curve. An exact definition cannot be given as normotension and hypertension. The best operational definition is the level at which benefits of action exceeds the risks and costs of inaction due to hypertension.

As per JNC VII (2003) report hypertension is defined as systolic ≥140mmHg and or diastolic ≥ 90mmHg. The JNC classification for blood pressure in persons aged >18 yrs is provided in Table 2:

Table 2: JNC classification for blood pressure*

BP classification	SBP mmHg		DBP mmHg
Normal	<120	and	<80
Pre hypertension	120-139	(or)	80-89
Hypertension Stage I	140-159		90-99
Stage II	≥160		or ≥100

*** Source:** 7th report of Joint National Committee on the prevention, detection, evaluation and treatment of high blood pressure (JNC VII). Chobanian AV,

Bakris GL, Black HR, Cushman WC, Green LA. Hypertension 2003. Dec; 42(6) 1206-52.

Natural history of untreated hypertension

The pathological hallmark of hypertension is the accelerated atherosclerotic rigidity of large capacitance arteries which is evident by rising systolic and falling diastolic levels. The resultant widening of pulse pressure is said to be the best prognostic indicator for cardiovascular risk.

The MRFIT study had showed that each 20mmHg rise in systolic blood pressure and 10mmHg rise in diastolic pressure is associated with more than two fold increase in mortality from stroke and coronary artery disease[13].

Mechanisms of essential hypertension

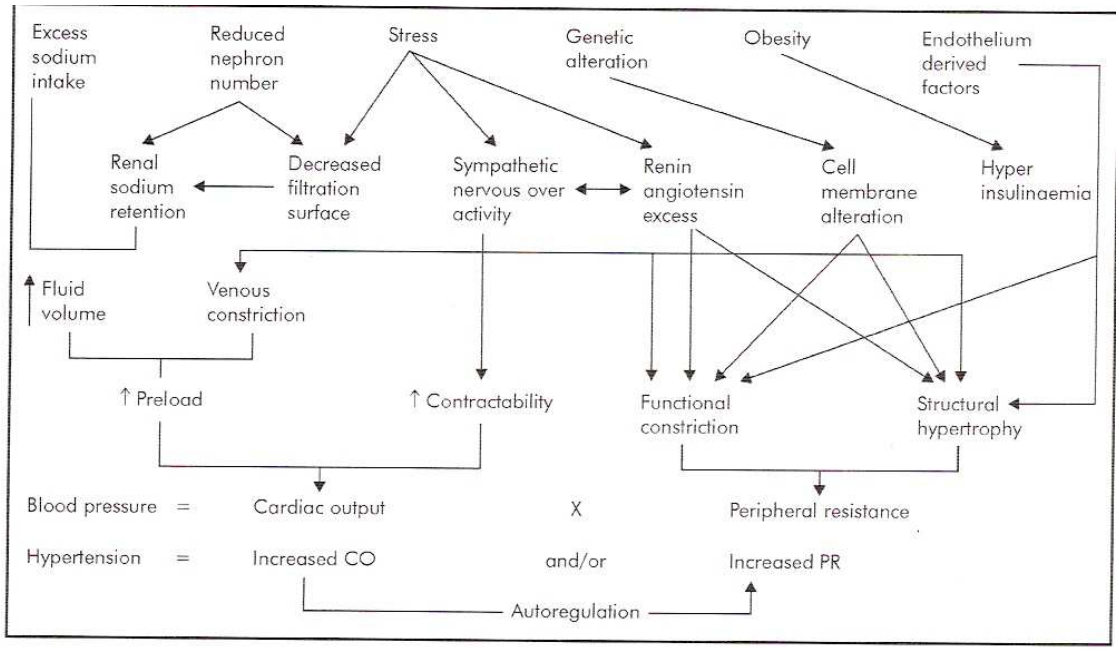
1. Hemodynamics

Blood pressure is the pressure required to move blood through the circulatory bed by pumping action of the heart and the tone of the arteries.

Blood pressure (BP) = cardiac output × peripheral resistance

Any factor which influences the above two factors could cause an increase in blood pressure.

Fig 2: Factors determining blood pressure*



*** Source[14]:** Vikrant S, Tiwari SC: Indian Academy of Clinical Medicine Journal 2001; 2(3): 14-157.

Regardless of how hypertension begins, eventually increased peripheral resistance becomes the primary hemodynamic facet of sustained hypertension.

2. Role of Genetics

Family aggregation of blood pressure has been demonstrated in family members and twins. Essential hypertension is almost certainly a polygenic disorder, involving multiple genes, each having a small effect on the blood pressure[15]. Along with this multiple environment factors play a role interacting with the genes to skew the distribution of blood pressure to higher levels[16].

The identification of various genes that contribute to the development of hypertension is complicated by the fact that the 2 phenotypes that determine blood pressure i.e., cardiac output and total peripheral resistance are in turn controlled by intermediary phenotypes including the autonomic nervous system, vasopresssor and vasodepressor hormones, the structure of the cardiovascular system, blood volume and renal function and many others[17].

Mutations in genes such as angiotensin gene, β2 adrenergic receptor, Adducin, renin binding proteins, G-protein β3 subunit, atrial natriuretic factor and insulin receptor has been linked to the development of essential hypertension, but most of them only show a weak correlation[14].

3. The Fetal Environment

Low birth weight has been found to be followed by an increased blood pressure[18].

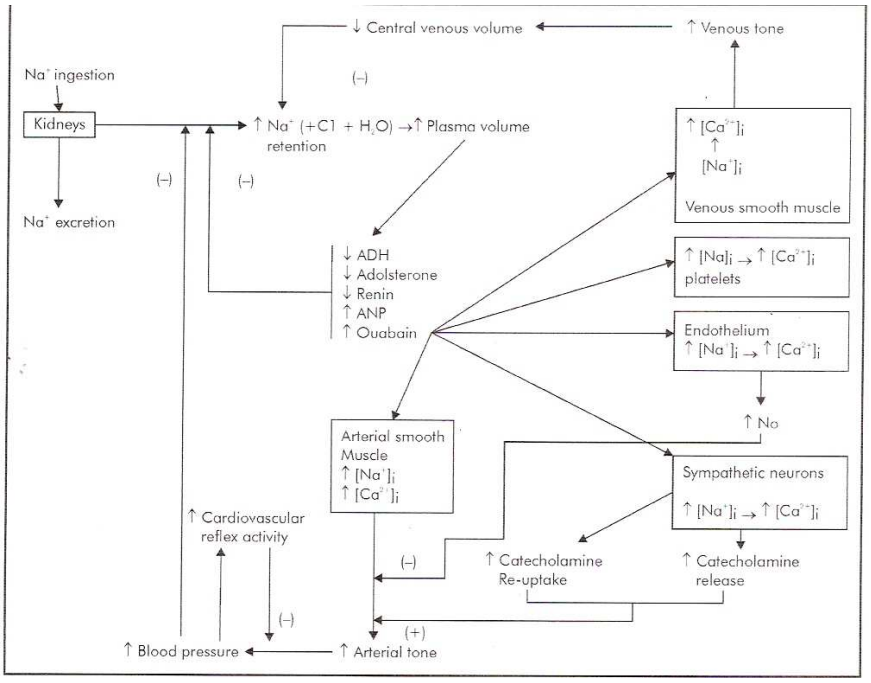
Despite objections of this theory Brenner and his colleagues hypothesized that IUGR affects nephrogenesis and this low number perhaps eventuates hypertension.

4. Sodium and the Kidney

Essential hypertension is primarily due to an abnormal kidney which has an unwillingness to excrete sodium[19]. The contribution of sodium to blood pressure is probably due to sodium retention, the mechanisms by which it retains sodium are provided below and the same has been depicted in a pictorial manner in Fig. 3.

- A decrease in the filtration surface by a congenital or acquired deficiency in nephron number or function[20].
- A resetting of the pressure natruiesis and pressure diuresis mechanisms[21]
- An acquired inhibitor of sodium pump[22]
- Nephron heterogeneity: The presence of subgroup of ischemic nephrons either from afferent arteriolar vasoconstriction or from an intrinsic narrowing of the lumen[23].

Figure 3: Sodium and blood pressure*



*** Source:** Vikrant S, Tiwari SC: Indian Academy of Clinical Medicine Journal 2001; 2(3):140-157.

5. Vascular hypertrophy

A number of factors increase peripheral resistance by functional contraction, vascular remodelling and hypertrophy. These pressor growth promoters may result in both vascular contraction and hypertrophy simultaneously, but perpetration of hypertension involves vascular hypertrophy. Hormonal mediators such as angiotensin II and endothelin may serve as the initiator events to an increased peripheral resistance. Lever and Harrap postulated that essential hypertension is alike secondary hypertension in its history and has two stages

1. Growth promoting process in children

2. Self perpetuating mechanism in adults[24].

6. Renin - Angiotensin system

Renin acts as a direct pressor and a growth promoter and is likely to be involved in the pathogenesis of hypertension, when sodium intake is reduced or effective plasma volume shrinks. The increase in renin – angiotensin II stimulates aldosterone secretion which in turn is responsible for renal retention of sodium and water in essential hypertension. In contrary to the expectation the plasma renin activity is low only in 30% of patients whereas 50% have normal levels and the remaining 20% have high levels[5].

Three mechanisms have been suggested for the above phenomenon

- Nephron heterogeneity
- Non modulation
- Increased sympathetic drive

7. Sympathetic nervous hyperactivity

Young hypertensive patients tend to have increased levels of circulating catecholamines, augmented sympathetic nerve signals in muscles, faster heart rate, and heightened vascular activity to alpha adrenergic agonists[25].

In the Framingham study in middle aged men over an 18 to 20 year period hypertension was more common in patients with heightened anxiety, suppressed expression and anger at baseline[26].

These changes increase blood pressure by various mechanisms like an increase in renin release, increased cardiac output (or) by altering the nocturnal renal pressure – volume relationship.

8. Hyperinsulinemia / Insulin resistance

Hypertension, hyperinsulinemia and obesity, especially obesity which is predominantly visceral and in the upper abdomen is a well known dangerous trio. The presence of hyperinsulinemia and insulin resistance[27] is seen in about 20% of non obese hypertensives.

The exact cause of insulin resistance in non-obese hypertensive persons is not known. It could simply reflect a reduced ability of insulin to reach the skeletal muscle cells, where the major peripheral action of glucose occurs. (This impairment may in turn result from a defect in the vasodilatory effect of insulin).

Insulin has multiple pressor effects including activation of sympathetic activity, trophic action on the vascular system causing hypertrophy and increase in renal sodium absorption. Normally the pressor effects are counteracted by insulin mediated increased synthesis of nitric oxide. In hypertension there is impairment in the insulin mediated increase in nitric oxide leading to a rise in the blood pressure.

9. Endothelial dysfunction

Nitric oxide

A reduced vasodilatory response to various stimuli of nitric oxide release appears to be an independent factor for the origin of essential hypertension[28].

Endothelin

Endothelin -1 appears to be of particular importance because it causes pronounced and prolonged vasoconstriction and blockade of its receptors. Also, it improves endothelium dependent vasodilation in hypertensive patients, but its role in human hypertension is debatable[29].

10. Other possible mechanism / associations

Hypertension is associated with obesity, sleep apnoea, physical inactivity, alcohol intake, smoking, higher haematocrits, hyperlipidemia and hypercholesterolemia[5].

TARGET ORGAN DAMAGE

Target end organ damage can be defined as the organs affected by hypertension due to the increase in the blood pressure[30].

Hypertension and the heart

It can be classified into

1. Left Ventricular hypertrophy
2. Systolic and diastolic dysfunction

Hypertension causes more than double the risk for symptomatic coronary disease, including acute myocardial infarction and sudden death and more than triples the risk for congestive heart failure[31].

The consequences reflect an admixture of effects induced by hypertrophic response of the left ventricle to the increased after load imposed by hypertension.

Left ventricular Hypertrophy

This is the most important cardiac abnormality in hypertension. The normal left ventricle grows from infancy until adulthood[32]. Further increase may occur according to the haemodynamic load.

a. Normal Left Ventricular size

Body surface area is generally taken into account for the left ventricular mass index, which was reported by Cornell and Framingham as 134gm/m^2 and 131gm/m^2 in males while in females it was 109g/m^2 and 100gm/m^2 respectively[33,34].

The gender difference may reflect genetic, hormonal or exercise effects that influence both skeletal and heart muscle. Relation between age and left ventricular dimension or mass is either weakly positive or absent[35].

Prevalence

Left ventricular hypertrophy is identified by ECG in only 5 to 10% of hypertensives but left ventricular hypertrophy by echocardiography is seen in nearly 30% of unselected hypertensive patients[36].

Fundoscopic changes (or) other target organ abnormalities used to classify patients as having stage 2 hypertension under WHO scheme have a high prevalence of echocardiographic left ventricular hypertrophy in one series of hypertensive patients.

The prevalence of left ventricular hypertrophy among hypertensive patients is influenced by gender and obesity. Sex specific criteria for left ventricular mass index identifies left ventricular hypertrophy more in women than in men as used in the Framingham population study.

Pathogenesis / Factors influencing left ventricular hypertrophy

Although one might expect the elevated blood pressure would consistently induce left ventricular hypertrophy, the data reviewed doesn't indicate the case[37].

a. Blood pressure

Left ventricular muscle mass is usually more closely related to systolic blood pressure than diastolic. Left ventricular mass in hypertensive patients is more closely correlated with systolic blood pressure at the end of maximal exercise than with the resting systolic pressure[38].

A study in employed population revealed that blood pressure and left ventricular mass were high in jobs with high strain[39].

b. Haemodynamic volume overload

Supranormal cardiac output is a well documented phenomenon in high normal blood pressure and hypertension. Conversely low normal (or) subnormal cardiac output and stroke volume may occur with markedly elevated peripheral resistance in patients with relatively severe hypertension[40].

The important role of volume load in pathogenesis of hypertension and left ventricular hypertrophy is underscored by the fact that left ventricular chamber size and stroke volume are more closely related than systolic pressure to left ventricular mass in normotensive and mildly hypertensive humans[41].

c. Blood viscosity

Left ventricular thickness and mass are directly related to the whole blood viscosity, extending the previous documentation of Strandell of the heart volume and haemoglobin[42].

NON HAEMODYNAMIC STIMULI TO HYPERTENSIVE LEFT VENTRICULAR HYPERTROPHY

1. Sympathetic Nervous system

It is a controversial topic. The point favouring sympathetic nervous system and left ventricular hypertrophy is largely based on the concept that

hypertrophy is due to excess catecholamines, in laboratory experiments[43]. But the points that suggest sympathetic nervous system has only a limited impact on left ventricular hypertrophy are:

1. Haemodynamic pressure or volume load responses to adrenergic stimulation or blockade has not been characterised.
2. Catecholamines do not induce hypertrophy of cultured adult cardiac myocytes.
3. In patients with pheochromocytoma the state of hyperadrenergic hypertension have left ventricular hypertrophy that is proportional to their blood pressure and not to their catecholamine levels[44].

2. Renin – angiotensin system

This concept is of the changing trend. In the past an independent role of circulating or intracellular renin-angiotensin system in hypertensive left ventricular hypertrophy was to be proven and clinical studies found no difference in left ventricular mass among patients with high/normal (or) low renin forms of essential hypertension[45].

But the present day trend is that there is a close correlation between the circulating levels of renin with left ventricular mass[46] by the recognition of a close connection between left ventricular hypertrophy and a deletion

polymorphism of the angiotensin converting enzyme gene the DD genotype, which increases plasma angiotensin converting enzyme activity[47]. The involvement of RAS and heart is further strengthened by the impressive effect of ACE inhibitors on the regression of left ventricular hypertrophy and remodelling of the heart after MI[48].

3. Increased Left Ventricular mass as a precursor of hypertension

The possibility that left ventricular hypertrophy is not only a consequence but could also precede it[49] was first raised by the observation that base line left ventricular mass in children and adults contribute independently to predicting their blood pressure 4 years later.

The strongest predictor of subsequent hypertension was the initial left ventricular mass with additional independent prediction by the 24 hour urinary sodium/potassium excretion ratio[5].

Relation between cardiac and vascular changes in hypertension

Increased vascular resistance and vascular hypertrophy have been related to left ventricular adaptive changes but not in all studies. Geri *et al* found a weak but significant relation between calf vascular resistance and left ventricular mass[50].

Schulte *et al* found a significant relation between forearm vascular resistance and left ventricular mass in hypertensive patients[51].

Patterns

The left ventricular hypertrophy may occur in any of the following forms. Concentric, eccentric remodelling (or) concentric remodelling or the mass may not be increased.

Consequences of hypertensive hypertrophy

Increased left ventricular mass is a potent predictor of cardiovascular morbidity and mortality, independent of blood pressure or other risk factors.

The Framingham heart study concluded that only left ventricular mass index and age were strong and consistent predictors of all the above.

Systolic and diastolic dysfunctions[5, 30]

In contrast to general normality of systolic left ventricular performance in uncomplicated hypertension, left ventricular diastolic filling is abnormal in many adults.

Characteristically early diastolic left ventricular filling is impaired with normal (or) enhanced filling during atrial systole, identifying subnormal left ventricular relaxation but not compliance. Notably impaired left ventricular diastolic relaxation occurs in patients in whom extreme left ventricular hypertrophy with preserved systolic function is complicated by heart failure and reduced early diastolic left ventricular filling is strongly related to left ventricular mass. But diastolic left ventricular filling may also be abnormal in

hypertensive patients with normal left ventricular anatomy and is usually normal in athletes with hypertrophy.

In established hypertension, abnormal relaxation has been observed in $2/3^{rd}$ of patients with normal left ventricular systolic function.

The spectrum of diastolic dysfunction courses on one end, from the failure of left ventricular end-diastolic volume to rise appropriately with exercise, all the way to the other end of left ventricular heart failure with normal systolic function with diastolic heart failure.

Systolic dysfunction

In mild to moderately hypertensive patients left ventricular systolic performance at rest is normal (or) mildly increased. But it has been shown that left ventricular ejection fraction and fractional shortening measured at the endocardium to be normal (or) supranormal may reflect a “conceptual mismatch”. When the midwall shortening and end diastolic stress relations were analysed in relatively unselected hypertensive patients with concentric left ventricular hypertrophy, decreased myocardial contractility and no significant hypercontractility was observed in patients without left ventricular hypertrophy. In recent large studies a depression of left ventricular systolic function was found in 8.9-17.5% of patients.

THE KIDNEY

The number of patients developing end stage renal disease secondary to hypertension is increasing and the mechanism involved in the sclerotic processes are not only a sequel of hypertension, but also contributes to its pathogenesis.

Looking back, Gull and Sutton were the first to suggest that a vascular disease has a primary pathologic role in hypertension. Jores in 1904 provided the anatomic basis for differentiating primary and secondary hypertension[5].

Various theories have been proposed about the kidney and hypertension[5]

1. Renal disease is primary and that the associated vascular disease and hypertension were its results.
2. Renal disease is a part of a primary vascular disease and the progressive vascular sclerosis increases peripheral resistance, resulting in systemic hypertension.
3. Essential hypertension itself is a primary disease and the vascular diseases seen in all organs are a result rather than a cause.

Whatever the theory may be but it is clear that vasculopathy of hypertension is a distinct and perhaps unique lesion which involves the kidney preferentially.

Microvascular disease of the kidney[5]

The vessels most susceptible to hypertension are the small arteries, arterioles and the preglomerular vessels tend to be more prominently affected than that of the postglomerular arterioles.

The vascular pathology of the small arteries and arterioles of the kidney falls into 3 general categories.

1. Hyaline arteriolar sclerosis
2. Myointimal hypertrophy and hyperplasia
3. Fibrinoid necrosis

The first form occurs in all forms of hypertension while the second and third are hallmarks of malignant hypertension.

We would see a few words about hyaline arteriolar sclerosis because the other two are hallmarks of malignant hypertension.

Hyaline arteriosclerosis

The most interesting microvascular pathology is hyaline arteriosclerosis.

This deposition of hyaline in small arterioles causes atrophy of the smooth muscle cells and irregular thickening of the basement membrane.

Hyaline arteriosclerosis may be associated with aging but are usually minimal and focal and are not associated with elevations of diastolic blood pressure.

The presence of hyaline is unrelated to age and it is related to both severity and duration of hypertension.

The deposition of hyaline at the end, may result in a more or less fixed vascular lumen leading to an elevation of peripheral vascular resistance and relative – ischemia of the regions supplied by the vessel.

Whatever may be the pathology it ultimately leads to albuminuria followed by nephrosclerosis.

Albuminuria[52]

It is now accepted that microalbuminuria is a more generalized vascular problem and not just confined to the renal microcirculation.

An increase in urine albumin above the normal 30mg/dL is defined as albuminuria. Microalbuminuria is used to define smaller degrees of albuminuria (30-300mg/dL). False positive results may be observed in the presence of alkaline urine and following radio-contrast administration.

Pathophysiology

The glomerular capillary wall provides a barrier to the filtration of large macromolecules. The barrier to filtration is provided by 2 mechanisms.

1. Size selectivity

2. Charge selectivity

Size selectivity

The endothelial cells have fenestrations with an approximate radius of 40nm and as such do not provide an effective barrier to albumin. The glomerular basement membrane and the foot processes of epithelial cells serve as the major components of size selectivity.

Charge selectivity

The anions on the GBM provide the charge selectivity. Loss of the negative charge may result from the disruption of the epithelial cell barrier and may lead to albuminuria.

When there is damage to the basement membrane or components of the glomerular epithelial cells, often the first manifestation is the appearance of plasma proteins in the urine because albumin is the major circulating protein in plasma. Its appearance in the urine is the most sensitive indicator of disruption of the glomerular filtration barrier.

In both hypertensives and normotensives, the presence of microalbuminuria is correlated to the presence of left ventricular hypertrophy and the presence of microalbuminuria predicts increased risk of cardiovascular morbidity and mortality[53]. It has also been shown that there is a greater risk of hypertensive retinopathy and progressive atherosclerosis[54].

Incidence of microalbuminuria

The prevalence of microalbuminuria has been reported with variation between 5 and 37%.

Factors determining albuminuria

1. **Genetic**

   No specific gene could be positively correlated, but chromosome 10q has been implicated.

2. **Race**

   Albuminuria is more common in African Americans / American Indians and Hispanics in western literature. There is no study in our population about the incidence of albuminuria.

3. **Sex**

   It is twice more common in males than in females.

4. **Age**

   Persistent albuminuria increases with age.

5. **Blood pressure**

   There is increased albuminuria with increasing blood pressure.

Despite the strong epidemiological evidence of the association between hypertension and renal disease some authors question their relationship because randomized controlled trials have shown that the renal dysfunction developed infrequently during various treatment schedules of hypertension[30].

However, it should be remembered that renovascular diseases are not an infrequent cause of renal insufficiency and hypertension.

THE EYE

Patients with only hypertensive retinopathy are nearly always visually asymptomatic. In many instances the hypertension may be unknown to the patient and the eye examination may yield the first clue to this relatively asymptomatic disease[55].

Elevation of systemic blood pressure causes both focal and generalized retinal arteriolar constriction, presumably mediated by autoregulation. A prolonged duration of particularly high blood pressure can be associated with a break down of the inner blood retinal barrier, with extravasation of plasma and red blood cells. Retinal haemorrhages, cotton wool spots (micro-infarcts), intra retinal lipid accumulation and in severe cases the development of a macular star may be seen[55].

In severe hypertension, closure of retinal capillaries are observed. When the choroidal vessels are severely affected by elevated blood pressure, as in acute hypertension, fibrinoid necrosis of choroidal arterioles can cause occlusion, with subsequent break down of outer blood retinal barrier.

The relationship between pure hypertensive changes and arteriosclerosis are so complex that it is impossible to consider them separately[55].

A method of objectively evaluating retinal vessel calibres is from digitized fundus photographs.

The Beaver Dam study showed that narrowed retinal arterioles are associated with long term risk of hypertension suggesting structural alterations of the microvasculature may be linked to the development of hypertension. The Blue mountain eye study showed that the arteriolar narrowing of retinal vessels was a consequence of hypertension[55].

The presence of hypertensive retinopathy diagnosed clinically was correlated with doubling of the risk of coronary heart disease events.

Retinal changes and hypertension[55]

a. Arteriolar narrowing

Diffuse arteriolar narrowing is a hallmark of hypertensive retinopathy. Although it can be seen as an acute vasospastic response to acute hypertension, it is more commonly seen in chronic hypertension. The reduction in the caliber of arterioles is largely responsible for the reduction of arteriole to venule ratio associated with hypertension.

Focal arteriolar narrowing is attributed to localized areas of spasm of arteriolar wall and can be reversible. Persistent focal arteriolar narrowing may be due to oedema in the wall of the arteriole or localized area of fibrosis.

b. Arteriosclerosis

Hypertensive arteriosclerosis refers to the progressive increase in the elastic and muscular components of the wall of arteriole induced by long standing hypertension. With advancing age the same changes can occur and this is called as involutional arteriosclerosis.

c. Sclerotic changes

Increased thickening of the arteriolar wall caused by the arteriosclerotic processes causes progressive change in the appearance of light reflex from arteriole. Normally the arteriolar wall is invisible, only a column of red blood cells in the lumen is visible, and this appears as the red line we recognize. As the wall becomes thickened, the light reflex loses its brightness and becomes broader, duller and more diffuse in nature. This is the earliest sign of arteriosclerosis.

With increasing thickening of the arteriolar wall and decreasing lumen the light reflex takes on the reddish-brown hue of the ‘copperwire’ reflex. As the process continues, there is further thickening of the arteriolar wall with associated reduction in the lumen. The arteriole assumes the appearance of a silver wire, when the column of blood can no longer be visualized.

Arteriosclerotic thickening of the vessel wall also affects the appearance of arteriolovenous crossing. The vascular sclerosis and glial proliferation contribute to the compression of the venule and constriction of its lumen, causing the appearance of arteriolovenous nicking.

The sclerotic changes can also cause deflection of venule as it crosses the arteriole.

Hypertensive choroidopathy and hypertensive optic nerve changes are seen in longstanding hypertension.

Classification of hypertensive and arteriosclerotic changes[55]

Two popular classifications are

1. The Keith – Wagener – Barker classification (1939) – based on the level of severity of retinal findings.
2. Scheie's (1953) classification to quantify the changes of hypertension and arteriosclerosis separately in a five – stage classification.

Central nervous system[56]

Hypertension is more strongly correlated with stroke than with heart diseases.

Cereberovascular accidents

In hypertensives, nearly 80% strokes are ischemic, 5% are subarachnoid haemorrhage and 10 to 15% intra-parenchymal haemorrhage.

Isolated systolic hypertension in the elderly is associated with 2-4 times greater incidence of stroke than is seen in normotensive people of the same age.

Cognitive impairment and dementia[30]

Hypertension is associated with impaired cognition in the absence of clinically evident cerebrovascular disease[30].

Cognitive impairment is related to hypertension atleast upto the age of 70 after which the relationship decreases.

Other end organ damages[30]

Large vessel disease such as abdominal aortic aneurysm, aortic dissection, peripheral vascular disease and Takayasu's disease are all related to hypertension and regarded as target organs of damage.

MATERIALS AND METHODS

I. Type of study	:	Observational study
II. Setting	:	Department of Medicine Government Rajaji Hospital Madurai.

III. Collaborating Department	:	Department of Cardiology Madurai Medical College, Madurai.
IV. Duration of Study	:	January 2005 – December 2005
V. Ethical clearance	:	Ethical clearance was obtained. A Copy of the letter is enclosed in Annexure I.
VI. Consent	:	Informed consent was obtained before taking up each case for study
VII. Inclusion criteria	:	All newly diagnosed rural essential hypertensives of both sexes who were conscious, cooperative and free of overt comorbid illness were considered for the study.
VIII. Exclusion criteria	:	Patients who had any of the following were excluded from the study.

1. Age <25 or >75
2. BMI <18 or > 25

Cardiovascular system and respiratory system

3. Patients with primary cardiac (or) pulmonary disease
4. Patients with secondary hypertension

Renal system

5. Patients with macroalbuminuria / urinary infection
6. Patients with renal failure
7. Renal transplant patient

Endocrine

8. Patients with diabetes
9. Patients with thyroid disorders or adrenal disorders

Acute condition

10. Acute myocardial infarction
11. Acute cerebrovascular accident
12. Acute medical emergencies or urgencies

Others

13. Patients with malignancy
14. Bed ridden patients
15. Psychiatric patients
16. Uncooperative patients

17. Pregnant women
18. Women on oral contraceptive pills
19. Living in Madurai city or any urban area

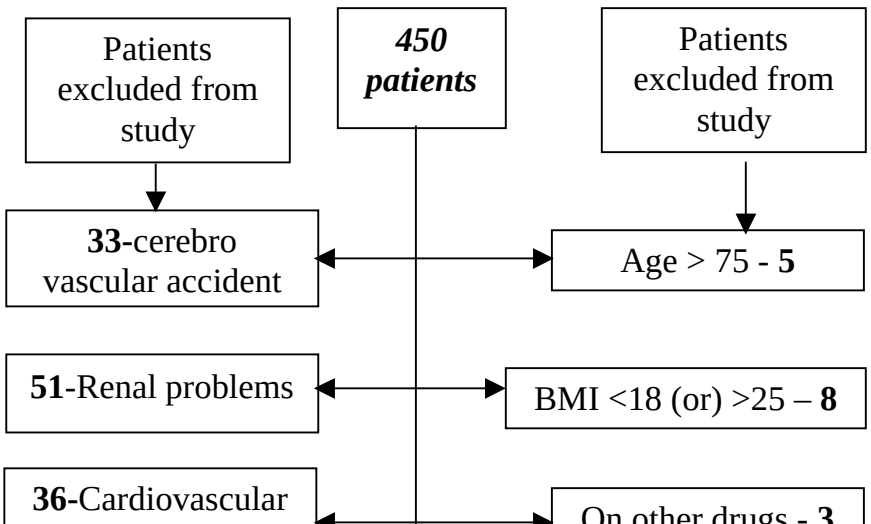
Habits

20. Patients who are alcoholics /smokers
21. Patients who are on drugs / diuretics

IX. Materials

A total of one hundred and forty seven (n=147) consecutive patients of newly diagnosed essential hypertension, attending the outpatient Department, of the Department of Medicine, Government Rajaji Hospital, Madurai were included for this present study based on a set of inclusion and exclusion criteria out of 450 persons seen. The exclusion of other patients is given in Figure 4 below:

Figure 4: Patient flow chart



X. Methods

Selected socio-demographic, clinical and laboratory data were elicited from these patients and recorded in a proforma.

1. Socio-demographic data
    - Age

- Sex
- Health seeking behaviour

2. Clinical data
    - Clinical history was elicited in detail with special emphasis on headache, giddiness, palpitation, breathlessness, chest discomfort, swelling of legs, sexual dysfunction, sleeplessness etc.,
    - Systolic and diastolic blood pressure were measured using standard procedures. The procedure used to record systolic and diastolic blood pressures is detailed below.
    - Clinical examination with special attention for thyroid swelling, renal bruit, cardiac murmur and additional sounds.
3. Laboratory data
    - Blood urea: Estimation done manually using diacetyl monoxime (DAM) technique.
    - Serum creatinine: Estimation was done using COBAS autoanalyser.
    - Blood Glucose: Estimation was done using COBAS autoanalyser.
    - Urine for microablumin: ELISA immunometric assay was used and read with NYCOCARD Reader II. The patients were explained the importance of bed rest and over night urine collection to avoid physiological and pathological variations.

Single channel Electrocardiogram was done to measure the electrical activity of the heart. Echocardiogram was carried out at the Department of Cardiology for every case to assess the cardiac function and status. The parameters studied were

1. Diastolic function indices
    a. Deceleration Time (DT)
    b. Iso Volumetric Relaxation Time (IVRT)
    c. Mitral E deceleration time
    d. Mitral E and A velocities
2. Systolic function indices
    a. Ejection fraction (EF)
3. Left Ventricular Mass

Eye

An amydriatic ophthalmoscopic examination was done in all patients for hypertensive retinopathy.

XI. Conflict of Interest : Nil

XII. Financial support : This study did not receive any financial support from any organization.

Data were entered in a predetermined proforma and later entered into a Microsoft excel spread sheet and analysed using SPSS Package.

XIII. Limitations of the study

1. As the inclusion criteria were rigid, the true number of cases will be more than the number of cases reported during the study period.
2. Histopathological examination could not be done since the ethical committee did not approve for renal biopsy as it is an invasive procedure.
3. As the hospital caters to low socioeconomic status people, BMI of these patients were <20. BMI was not correlated with the severity of target organ damage in the study population.
4. Due to technical constraints, complete profile of lipids was not carried out.
5. Elaborate investigations to exclude secondary hypertension could not be carried out due to technical constraints.

XIV. DEFINITIONS USED FOR THE STUDY PURPOSE

1. Essential hypertension

Hypertension was defined in accordance to the JNC-VII report[1] as systolic blood pressure of 140mmHg and above, and (or) diastolic pressure of

90 and above. The newly diagnosed patients were identified by the mean of 3 relaxed, seated right arm readings. The diagnosis that the hypertension was essential and not secondary was made on the overall clinical impression only.

2. Microalbuminuria

An overnight sample of urine was taken and a value of 20-200mg/L was defined as microalbuminuria.

3. Hypertensive retinopathy[55]

Based on Keith-Wagener-Barker classification.

I. There is minimal constriction of the retinal arterioles with some tortuosity.

II. Retinal abnormalities include those of group I with more definite focal narrowing and arteriolovenous nicking in patients with minimal or other systemic involvement.

III. Abnormalities of I and II along with hemorrhages and exudates and vasospastic changes, including focal arteriolar constriction and cotton wool spots.

IV. The abnormalities listed above are present and are usually more severe and there is optic disc oedema, Elsching's spots are present in some.

Left ventricular hypertrophy

Electrocardiography

Based on the electrocardiography satisfying either Sokolow-Lyon criteria or Cornell voltage criteria[57, 58].

Echocardiography

A left ventricular mass of 136 gm/m^2 for males and 112 gm/m^2 for females were taken as upper limit of normal values. Any value higher than the above values were taken as left ventricular hypertrophy.

Diastolic dysfunction[59]

Normal mitral E/A: 1-2, values less than 1 were taken as diastolic dysfunction.

Deceleration Time: 160-240 m/sec. Values greater than 240 m/sec. indicated diastolic dysfunction.

Intraventricular Relaxation Time: 70-90 m/sec. Values greater than 90 m/sec. indicated diastolic dysfunction.

Systolic dysfunction[60]

An ejection fraction of 50-80% was considered within normal limits. Values less than that were considered as systolic dysfunction.

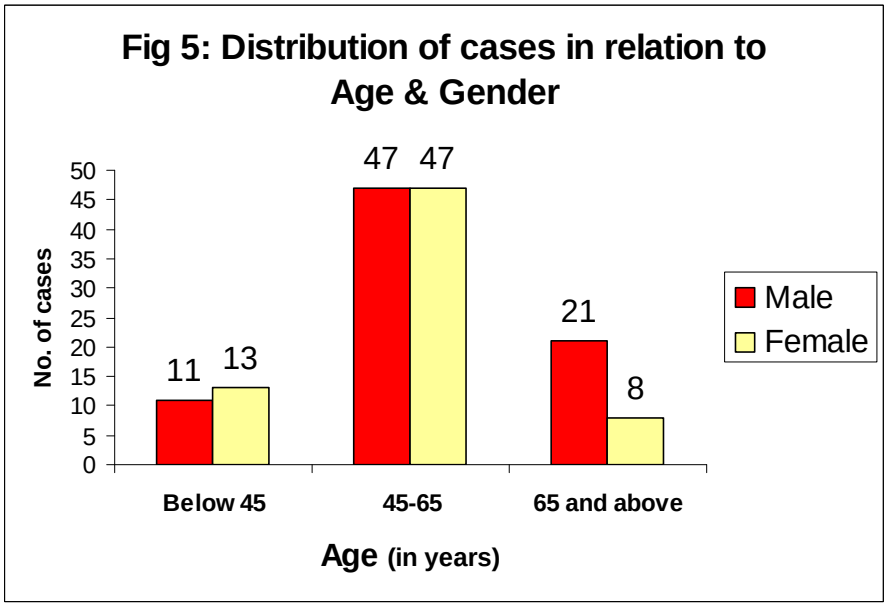
RESULTS

A total number of 147 newly diagnosed essential hypertensive patients were studied. The 147 patients were categorized into 3 groups as per the age classification adopted by WHO.

Table 3: Distribution of cases in Relation to Age & Gender

Category	Age Group	Male	Female	Total
Young	Below 45	11 (13.9%)	13 (19.1%)	24 (16.3%)
Middle Age	45-65	47 (59.5%)	47 (69.1%)	94 (63.9%)
Elderly	65 and above	21 (26.6%)	8 (11.8%)	29 (19.7%)
Total	-	79 (53.7%)	68 (46.8%)	147 (100%)

In the table the percentage is divided in such a way that the total of all males and female are made upto 100%. The above is depicted in a pictorial manner below in fig 5.



The age range, median, mean, SD of the study population are provided in Table 4 below:

Table 4: The Statistical Analysis of the Age and Gender

	Male	Female	Total
Mean	56.77	52.55*	54.82
SD	10.16	9.15	9.90
Range	28-74	29-74	28-74
Median	56	52	54

* not significant

There was no significant statistical variation in the age of the patients taken into the study. Sub analysis with reference to age and gender also did not show any significant difference.

Blood Pressure Analysis

Of the 147 patients studied, 23 patients had Isolated systolic hypertension of which 17 were male and 6 were female. The details of systolic

blood pressure, diastolic blood pressure and mean arterial pressure of these patients are provided in Table 5 below, and in Figures 6 and 7 (on the left side).

Table 5: The Analysis of Blood Pleasure in Respect to Gender

	Mean ± SD		**Median**		**Range**	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**
Systolic BP	163.57±15.51	167.26±15.77	162	168	140-200	140-210
Diastolic BP	95.27± 11.37	104.08±15.75	94	100	72-130	72-148
Total (All patients)	**Mean**	**Median**			**Range**	
Systolic BP	165.27±15.68	164			140-210	
Diastolic BP	99.34±14.72	98			72-148	
MAP	99.05±15.80	96.67			60-135	

MAP – Mean Arterial Pressure

Distribution of mean ± SD of systolic blood pressure, diastolic blood pressure and mean atrial pressure in relation to age group and gender are given in Table 6 below:

Table 6: The Age wise and Gender wise break up of mean

Blood Pressure levels

	Age group (in years)					
	Male			Female		
B.P.	**<45**	**45-65**	**>65**	**<45**	**45-65**	**>65**
SBP	152.36 ± 13.76	166.47 ± 15.93	162.75 ± 13.06	167.08 ± 12.80	165.87 ± 16.41	175.75 ± 15.24
DBP	99.63 ± 8.04	97.36 ± 11.00	88.28 ± 11.03	104.00 ± 17.60	105.23 ± 15.32	97.50 ± 15.55
MAP	85.94 ± 14.96	101.56 ± 16.10	104.09 ± 15.14	97.94 ± 11.91	95.71 ± 14.95	110.75 ± 14.06

All the patients belonged to low income group (as our hospital provides free service and used mostly by low socio economic group). Break up analysis in relation to gender revealed that diastolic blood pressure was significantly more in women patients. Interestingly, diastolic blood pressure was higher in women of all age groups and it was significant.

Joint National Committee classification of patients

The 147 patients in the study group were classified into 2 groups as per JNC VII guide lines. Classification of cases under JNC class and gender as well

as JNC class and age group are provided in Table 7 and 8 respectively. The same is provided in a pictorial manner in figure 8 (on left side).

Table 7: Classification of the Patients as per JNC VII Guidelines by Gender

JNC Class	Male	Female	Total
I	22(27.8%)	15(22.1%)	37(25.2%)
II	57(72.2%)	53(77.9%)	110(74.8%)

Table 8: Categorization of Patients as per Age and Gender according to JNC

Age Group	JNC Category					
	I		II		Total	
	Male	Female	Male	Female	Male	Female
<45	4 (18.2%)	4 (26.7%)	7 (12.3%)	9 (17.0%)	11 (13.9%)	13 (19.1%)
45-65	12 (54.5%)	10 (66.7%)	35 (61.4%)	37 (69.8%)	47 (59.5%)	47 (69.1%)
>65	6 (27.3%)	1 (6.1%)	15 (26.3%)	7 (13.2%)	21 (26.6%)	8 (11.8%)

Statistical analysis of patients by gender and age with JNC classification was not significant.

1. Microalbuminuria

A value of less than 20mg/L denotes there is no microalbuminuria, but a value of 20-200mg/L indicates microalbuminuria. Patients with macroalbuminuria were considered under exclusion criteria.

Out of the 147 persons, 51 (34.6%) had microalbuminuria. Their gender and age group distribution are provided in Table 9 given below:

Table 9: The Gender and Age wise Classification of Patients with Microalbumiuria

Age Group	Microalbuminuria		Total
	Male	Female	
<45	4 (16.4%)	4 (15.4%)	8
45-65	13 (52.0%)	19 (73.1%)	32
>65	8 (32.0%)	3 (11.5%)	11

Analyzing all the 147 patients, the amount of albumin excreted in the urine was found out, it had a mean of 35.54 mg ± 54.03 while the median was 14 (range 2-200).

Overall microalbuminuria was independent of age and sex.

- Statistical analysis was performed to find out whether microalbuminuria had any relationship with the systolic blood pressure, diastolic blood

pressure and mean arterial pressure using ‘t’ tests and there was no positive correlation.

Microalbuminuria and retinopathy

Statistical analysis was made to find out the relationship between retinal involvement and microalbuminuria, and it was identified that they were interdependent variables with statistical significance (p=0.001). The results of an ANOVA were 0.0002. The details of the relationship between microalbuminuria, retinal involvement and gender are given in Table 10.

Table 10: Gender wise Classification of patients with Retinal Involvement with and without Microalbuminuria

Micro albuminuria	**Retinal Involvement***								
	Grade 0			**Grade I**			**Grade II & III**		
	M (%)	**F (%)**	**Total (%)**	**M (%)**	**F (%)**	**Total (%)**	**M (%)**	**F (%)**	**Total (%)**
<20mg	18 (85.7)	22 (91.7)	40 (88.9)	31 (79.5)	14 (63.6)	45 (73.8)	5 (26.3)	6 (27.3)	11 (26.8)
>20mg	3 (14.3)	2 (8.3)	5 (11.1)	8 (20.5)	8 (36.4)	16 (36.2)	14 (73.7)	16 (72.7)	30 (72.2)

*p = 0.0001; ANOVA = 0.0002 (Microalbuminuria vs Retinopathy vs gender)

Microalbuminuria and left ventricular mass / diastolic function

Diastolic dysfunction in patients was considered taking mitral E/A as the main parameter.

Excretion of albumin in the urine is correlated with the level of left ventricular mass and the diastolic dysfunction of the left ventricle. The details are provided in Table 11and 12 respectively.

Table 11: Relationship of Microalbuminuria with Left Ventricular Mass

S.No	Micro albuminuria	No of Patients	Mean LV mass	S.D.	t Value	p value
1	Normal	96	239.61	71.29	0.215	0.034
2	Abnormal	51	268.00	78.51		

Table 12: Mitral E/A's relationship to microalbuminuria

	Mitral E/A	Micro albuminuria	S.D.	t Value	p value
Normal	96	1.646	0.522	2.51	0.014
Abnormal	51	0.9527	0.469		

Left ventricular mass was greater in patients who had microalbuminuria than without and the difference was significant. Similar significance was noted with left ventricular diastolic dysfunction.

Using Chi square test and ‘t’ test it was found that Intraventricular relaxation time and Deceleration time were inter related.

Taking into account symptoms such as breathlessness, giddiness, chest discomfort and headache as comparable variables with microalbuminuria, a chi-square test was performed and none of the symptoms were positively correlated.

2. RETINOPATHY

Out of the 147 persons in the study group, 102 (72.1%) of persons had retinal involvement. In the study Keith – Wagener – Barker classification was used. 45 persons had no retinopathy, 61 persons had Grade I retinopathy, 38 persons had Grade II retinopathy, 3 persons had Grade III retinopathy and none had Grade IV retinopathy. The distribution of cases in relation to age and gender is shown in Table 13 (on the left side).

Age group statistical analysis with retinopathy found no significance in the young and middle age groups. But significance between old age and retinopathy was found in the study group.

Analysis was done to see whether gender had any role in modifying retinal changes in hypertension and the analysis showed that gender had no role in altering the changes in the retina among the newly diagnosed hypertensives.

The distribution of patients with or without retinopathy in relation to age group is given in Table 14:

Table 14: Retinopathy in relationship to Age Group

Retinopathy Grade	**Age Group* (in years)**		
	< 45	**45-65**	**>65**
0	12 (50%)	24 (25.5%)	9 (31.0%)
I	6 (25%)	48 (51.1%)	7 (24.1%)
II & III	6 (25%)	22 (23.4%)	13 (44.9%)

* significant (p=0.01)

A chi square test to find out the significance was performed for the total study group against retinopathy and a p value of 0.01 was obtained which is significant.

Retinal changes were analysed against left ventricular mass and the details in relation to gender is furnished below in Table 15. Retinopathy was significantly (p=0.0001) correlated with left ventricular mass.

Table 15: Retinopathy, Left ventricular mass and gender

Retinopathy Grade	LV Mass				Total		Mean LV mass (gms)
	Male		Female				
	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	
0	13 (46.4%)	8 (15.7%)	13 (68.4%)	11 (22.4%)	26	19	201.05
I	12 (42.9%)	27 (52.9%)	3 (15.8%)	19 (38.8%)	15	46	275.59
II & III	3 (10.7%)	16 (31.4%)	3 (15.9%)	19 (38.8%)	6	35	267.68
Total	28 (100%)	51 (100%)	19 (100%)	49 (100%)	47	100	248.10

There is a significant variation in left ventricular mass with retinopathy in grade II and III retinopathy but it is not significant when compared with grade I retinopathy. Their details in relation to gender are provided in Table 16 given below:

Table 16: Gender, Retinopathy and Left ventricular mass in gms

Retinopathy Grade	Male		Female		t value	p value
	No. of patients	Mean LV mass (gms)	No. of patients	Mean LV mass (gms)		
0	21	220.198	24	181.92	2.17	0.037
I	39	274.23	39	274.23	0.14	0.89
II & III	19	294.95	22	240.41	2.64	.013

a) Statistical analysis using ANOVA found the diastolic dysfunction (mitral E/A) was significantly correlated (p=0.00005) with changes in the retinal due to hypertension.

b) A chi square test performed with IVRT / Deceleration time against retinal changes found that they were positively correlated with significance values of 0.0001 and 0.00025 respectively.

c) Retinal changes were also analysed against giddiness, headache, breathlessness, chest discomfort, education and income status and was found to have no positive correlation.

Left Ventricular Mass

The analysis of left ventricular mass among the study population ranged from 83 to 409 gms. The mean and median were 249.46 ±74.85 gms and 260 gms respectively.

The left ventricular mass was calculated among male and female population. It was 264.85±71.79gm and 231.59±74.86gm respectively. The statistical analysis revealed that left ventricular mass was more in men and it was significant as shown in Table 17.

Table 17: Left Ventricular Mass and Gender

Gender	No. of Cases	Mean	t value	p Value
Male	79	264.85±71.79	2.74	0.007
Female	68	231.59±74.86		

There is a significant difference in the left ventricular mass between the male and female gender. However when age was correlated with left ventricular mass it was found to be independent of left ventricular mass.

Out of the 147 persons in the study, 100 individuals (68.0%) had left ventricular hypertrophy, which comprised of 51 males (64.6%) and 49 females (72.1%).

Left ventricular mass was not related to stage I of JNC (p=0.63) whereas a significant correlation with stage II JNC (p=0.01) was noticed. This indicates that when men progress to JNC class II their left ventricular mass increases. The details are provided in Table 18.

Table 18: Left Ventricular mass, JNC and Gender

S. No.	JNC	Gender				t value	p value
		Male		Female			
		No. of cases	Mean LV mass (gms)	No. of cases	Mean LV mass (gms)		
1	I	22	226.05	15	237.47	0.49	0.63
2	II	57	279.82	53	229.92	3.58	0.01

The number of cases of Left ventricular hypertrophy diagnosed by echocardiography was greater than that diagnosed by electrocardiogram. The difference was statistically significant (p=0.0003). The details are shown in Table 19.

Table 19: Electrocardiogram and Echocardiogram in relation to Left Ventricular hypertrophy

Echo cardiography	Electrocardiogram (RV6+SV1)		Significance
	<35mm	>35mm	
Normal	46	1	0.0003
Abnormal	73	27	

Analyzing left ventricular mass with deceleration time, intraventricular relaxation time and mitral E/A it was found that all the variables were interdependent with a significant correlation between them.

Symptoms and left ventricular hypertrophy

There was a significant correlation (p = .0.15) between left ventricular mass and giddiness (Table 20) but no association could be found with other symptoms such as headache, breathlessness and chest discomfort.

Table 20: LV Mass grouped and Giddiness

Giddiness	Left ventricular Mass		Significance
	Normal	Abnormal	
No	30	82	0.015
Yes	17	18	

Diastolic dysfunction

Diastolic dysfunction can be calculated using mitral E/A, deceleration time or intraventricular relaxation time. In this study it was analysed using mitral E/A. The patients in the study who had diastolic dysfunction had it of grade I only. The mean mitral E/A, and the median were 1.091±0.513 and 0.91 respectively. 86 persons (58.5%) had diastolic dysfunction, of which 53 (67.1%) were males and 33 (48.5%) were females.

Mitral E/A, Age group and Gender

When mitral E/A was analysed to find whether any correlation existed between age and gender, no association could be found out. The details are produced in Table 21.

Table 21: Gender, age group and mitral E/A

Age Group (in years)						**Mitral E/A**	**No of patients**
<45		**<45-65**		**>65**			
Male	**Female**	**Male**	**Female**	**Male**	**Female**		
4 (15.4%)	11 (31.4%)	17 (65.4%)	22 (62.9%)	5 (19.2%)	2 (5.7%)	>1	61 (41.5%)
7 (13.2%)	2 (6.1%)	30 (56.6%)	25 (75.8%)	16 (30.2%)	6 (18.2%)	<1	86 (58.5%)

Distribution of cases to IVRT and DT is shown in Table 22. The variables were significantly associated.

Table 22: Intraventricular Relaxation time (IVRT) and Deceleration Time (DT)

	Normal	**Abnormal**
IVRT	66 (44.9%)	81 (55.0%)
DT	75 (51.6%)	72 (49.0%)

A correlation matrix was made with retinopathy, microalbuminuria, left ventricular dysfunction (Mitral E/A) and left ventricular mass along with systolic blood pressure and diastolic blood pressure. The matrix is analysed in such a manner to find out which variable influences the other. The details are provided in Table 23 provided below:

Table 23: Correlation between major variables of the study

Correlation	**BP diastole**	**Retina**	**Micro albuminuria**	**Mitral E/A**	**LV mass**	**MAP**
BP Systole	0.2892**	0.2284*	0.1143	0.0393	0.0222	0.8186**
BP Diastole		0.1810	0.1215	0.0304	0.0661	0.3130**
Retina			0.3309**	0.2882**	0.3461**	0.1176
Micro albuminuria				0.2898**	0.2734**	0.0405
Mitral E/A					0.5807**	0.0208
LV mass						0.0176

2 tailed significance 0 .01* 0.001.**

Microalbuminuria:

It was not dependent on blood pressure levels, but it is positively correlated with retinal changes, diastolic dysfunction and left ventricular hypertrophy.

Retinal changes

There was positive correlation between retinal changes and systolic blood pressure but was not with diastolic blood pressure (or) mean arterial pressure.

The retinal changes, microalbuminuria, left ventricular mass and diastolic dysfunction are all interdependent variables.

Left Ventricular Mass

Overall there was no relation between Blood pressure and left ventricular mass, but a relationship of left ventricular mass with microalbuminuria and diastolic dysfunction was identified.

Diastolic Dysfunction

A relationship of mitral E/A with left ventricular mass and microalbuminuria was noticed, and no other factors influenced this variable.

None of the patients in the study group had systolic dysfunction.

Regression Equations

Regression equations were prepared to find out the left ventricular mass from microalbuminuria as well as electrocardiogram. The regression equations were formed taking the results obtained from the study.

1. *To find out left ventricular mass with microalbuminuria levels*

   Left Ventricular mass = 236.007 + (0.3786 x microalbumin level)

2. *To find the left ventricular mass from Electro cardiogram*

   Left Ventricular Mass = $181.278 + [2.860 \times (RV_6+SV_1)]$

Considering the whole study group of 147, the number of patients having one target organ damage or the other was observed in 126 (85.7%) of which males contributed to 70 while females were 56 in number, with a statistical significance among them (p=0.054). 21 (14.03%) cases did not have any target organ damage at all, while in 33 patients (22.4%) all the target organs screened were affected.

The target organ damage in relation to males and females are depicted in Figure 10 and 11 respectively (on the left side).

DISCUSSION

Hypertension is undoubtedly the most prevalent form of cardiovascular disease. It is present in nearly 25% of the adult population and the prevalence increases with age.

As the population becomes older and more obese, the incidence of hypertension continues to increase, and with the added disadvantage of the asymptomatic nature of the disease, it slowly but steadily damages the target organ (or) end organs i.e. the heart, kidneys, eye and the brain[30]. This is why Janeway and Walhard in the late 19th century aptly described Hypertension – "The silent killer"[61].

In this study only patients with normal BMI were taken, as obesity may be a contributory factor for hypertension. Smokers and alcoholics were also not included in the study since it may influence the rate at which target organ damage would occur as suggested by the LIFE study[62] in which smokers had an increased microalbumin excretion.

Out of the 147 patients, there were 79 males and 68 females; the mean age was 54.9±10.12 years. This is in contrast to other studies such as the MAGIC study[63] which had mean age of 51±0.06 years. Ceresola[64] *et al* reported a mean age of 44±0.5 years and Leoinci *et al*[65] reported 47±9 years. The difference in the mean age could be because of the late presentation of our

patients to the doctor. Late arrival may be related to the socio cultural reasons or belief in alternative systems of medicine.

The mean systolic blood pressure in the study was 165.27±15.68 and mean diastolic blood pressure was 99.34±14.72, but to the surprise the mean systolic blood pressure and diastolic blood pressure was more in females. It was about 5mmHg in systole but was not significant statistically, whereas a statistically significant variation of diastolic blood pressure (9mmHg) was noted in women.

Microalbuminuria

In the present study of 147 patients, 51 patients (34%) had microalbuminuria of which males contributed to 25 (of 79) and females contributed to 26 (of 68). There was no gender predominance and it was also independent of age in contrast to some of the published reports[65,67].

The MAGIC study reported a prevalence of microalbuminuria as 6.7%[63], while Agewall *et al* reported a 23% prevalence in patients undergoing treatment for hypertension[66]. Studies from Italy done by Leoncini[65] showed it to be as 13%, while a study in Madrid (Spain) by Martinez and his colleagues[67] revealed 7.2%. The LIFE study[62] and studies by Ponteremoli[68], showed prevalence rates of 23% and 14% respectively.

The prevalence of microalbuminuria found in western literature varied from as low as 4.7% to as high as of 40%[69]. Comparing with Indian statistics Ghai[70] reported a prevalence of 21.54%, but Jacob Abraham[71] had reported as prevalence of 58%.

A significant variability in the prevalence of microalbuminuria was attributed to the various values used to define it and the different techniques and protocols used to evaluate it. The prevalence of microalbuminuria was lower when only one overnight sample was taken for quantifying the result. A 24 hour urine collection would have given a higher value than an overnight sample because of the influence of food and physical activity on urinary albumin excretion. Due to the relative stability of renal haemodynamics at night, the results are reproducible with an overnight sample. So overnight sample collection was adopted in this study.

Since smokers and alcoholics were excluded from study population, it is likely that hypertension was the single most predominant risk factor to cause microalbuminuria in both genders.

In this study the blood pressure levels did not correlate with microalbuminuria levels in contrast to Martinez Maria[67] study group, hence it is likely that the duration of hypertension might have been contributed for glomerular changes, thus resulting in microalbuminuria.

Among the study group, a close relationship between retinal changes and microalbuminuria was noticed. Increasing grade of retinopathy as per Keith-Wagener and Barker classification, the probability of the patient developing microalbuminuria was greater. This was similar to that observed by Cuspidi *et al*[73]. Bisenbach *et al*[74] described a higher prevalence of coronary artery disease and hypertensive retinopathy in patients with persistent microalbuminuria.

The MAGIC study[63] also suggested that patients with microalbuminuria were characterised by diffuse vascular and target organ damage i.e. retinal changes.

This study revealed that the presence of retinopathy was more or less mandatory for the appearance of microalbuminuria.

Going by previous studies by Redon *et al*[75] who found out that patients with microalbuminuria showed a higher degree of left ventricular hypertrophy which was further confirmed by Cerasola *et al*[64]. Cuspidi *et al*[73] also found a positive correlation with microalbuminuria and left ventricular hypertrophy. From India Jacob Abraham[71] reported that proteinuria was significantly commoner in patients with left ventricular hypertrophy than in the control group.

Microalbuminuria when analysed in relation to left ventricular mass and mitral E/A independently, microalbuminuria was found to be directly proportional to left ventricular mass, but inversely proportional to mitral E/A.

A regression equation was also calculated from the study group having microalbuminuria and left ventricular mass. Using microalbuminuria levels left ventricular mass can be calculated using the formula in hypertensive patients.

Left Ventricular mass = 236.007 + [(0.3786) × microalbuminuria]

Diastolic dysfunction in the form of mitral E/A, IVRT (or) deceleration time had a significant correlation with the microalbuminuria.

RETINOPATHY

Prevalence

The prevalence of hypertensive retinopathy in this study was 72.1% and a comparative analysis of retinopathy in different series are provided in Table 24 given below:

Table 24: Retinopathy among Hypertensives

Study	Prevalence
Cerasola G *et al*[64]	54.83%
Jacob Abraham *et al*[71]	65.00%
Cuspidi C *et al*[73]	80.00%
Cuspidi *et al*[75]	80.00%
Present study	72.10%

In the present study there were no variations in the pattern of retinopathy in relationship with gender. A significant correlation of retinopathy was observed with old age, and no correlation was noted in the middle and younger age groups. The significance in elderly could be due to the arteriosclerotic changes combined with hypertension.

Retinopathy had a positive correlation (p=0.001) with left ventricular mass in this study, but Jacob Abraham *et al*[71] did not find any correlation between retinal changes and left ventricular hypertrophy.

The mean left ventricular mass was more in the Grade I hypertensive retinopathy group, than the group which had Grade II and III hypertensive retinopathy thus indirectly stating that additional factors like genetic factors might have influenced the appearance of retinal changes which needs further evaluation and confirmation.

Going on to analysis of left ventricular mass and retinopathy with gender, there was significant influence of the male gender with grade II and grade III hypertensive retinal changes put together, but it was not so in those with grade I hypertensive retinopathy. Retinal changes also correlated very well with diastolic dysfunction i.e. mitral E/A, intraventricular relaxation time and deceleration time. Retinal changes when analysed with the symptoms, no positive correlation could be obtained.

Cuspidi[76] and his co-workers suggested in their study that stage I and II hypertensive retinopathy were not associated with cardiac or extracardiac target organ damage, but in the present study even grade I and II retinopathy had been associated with significant target organ damage. Thereby indicating that duration of hypertension could have contributed for Target organ damage.

LEFT VENTRICULAR MASS

In this study the mean left ventricular mass among the 147 patients studied was 249.46±74.85gms. Among the males and females, left ventricular mass of 264.85±71.79, and 231.59±74.86 gms respectively, and further comparative analysis revealed a statistical difference (p=.007) among them. Out of the 147 patients, 100 patients (68%) had left ventricular hypertrophy.

Cuspidi *et al*[73] reported from Italy a prevalence of 22%, while Pontermoli reported from Italy a prevalence 47%[65], Jacob Abraham[71] from Bangalore, India reported a prevalence of 53% in hypertensive population. The higher prevalence noticed in this study would be due to the late presentation of these patients to the health sector.

When left ventricular hypertrophy was analysed with JNC classification there was no correlation of left ventricular mass with stage I, but there was a statistical relationship with stage II of JNC. This indicates that those with higher blood pressure are likely to have greater left ventricular mass.

As seen from literature increase in left ventricular mass causes diastolic dysfunction. A positive correlation between left ventricular mass with mitral E/A value, deceleration time and intraventricular relaxation time was noticed among the study population.

The study also concurred with a well known fact that echocardiogram is a better investigation than electrocardiogram to diagnose left ventricular hypertrophy.

Diastolic dysfunction

Diastolic dysfunction in this study was calculated using mitral E/A. There was no significant correlation of diastolic dysfunction with age and gender. Previous observation and a report by Marianne Hartford *et al*[77] revealed that greater the left ventricular mass the more the diastolic dysfunction. This study also goes in the same line.

Symptomatology

Zampaglione *et al*[78] reported some symptoms correlated with end organ damages. None of the symptoms could be positively correlated with target organ damage, other than giddiness which had an association with left ventricular mass ($p = 0.015$) in this study group.

Target Organ Damage

In this study, 126 persons (85.7%) of the 147 persons studied, had atleast one target organ damaged, it is much higher than that reported by Viazzi et al[79] from Italy who reported an incidence of 61%, this difference could be due to the late presentation our patient to the doctor.

Since one or other Target organ damage was observed in nearly all newly detected rural essential hypertensives, there is a urgent need to design and implement National Hypertension Detection and Control Programme by the Ministry of Health and Family Welfare, Govt. of India with the help of professional medical associations and non governmental organizations. It is time to act, better late than never, in order to prevent or minimize hypertension induced complications.

CONCLUSIONS

1. The prevalence of one (or) other Target organ damage was observed in 126 persons (85.7%) of the newly detected rural essential hypertensives.
2. The prevalence of retinopathy, left ventricular hypertrophy, diastolic dysfunction and microalbuminuria was observed in 72.1%, 68%, 58.5% and 34.6% respectively.
3. Microalbuminuria was significantly associated with retinopathy, higher left ventricular mass and diastolic dysfunction but not to age and gender.
4. Presence of microalbuminuria indicated widespread vascular damage.
5. Microalbuminuria was independent of blood pressure levels.
6. The study showed a correlation of retinopathy and systolic blood pressure, but not with diastolic blood pressure or mean arterial pressure.
7. Retinopathy had correlated positively with left ventricular mass and diastolic dysfunction irrespective of age and gender.
8. Left ventricular mass and diastolic dysfunction was inter-related.
9. When all Target organ damage were put together and were considered for gender difference, Target organ damage was significantly more among males (p=.054).

SUMMARY

Hypertension and target organ damage is a well known phenomenon. The study was undertaken to find the pattern of target organ damage in newly diagnosed non alcoholic, non smoking, non overweight, non dyslipidemic essential hypertensives of rural, low socio-economic status patients attending Government Rajaji Hospital, Madurai.

Thus 147 patients were taken up in the study group based on the rigid inclusion and exclusion criteria after institutional ethical clearance and an informed consent, out of 450 patients over a period of 12 consecutive months. Their sociodemographic, clinical and laboratory data were collected and analysed statistically.

There were 79 (53.7%) males (age range of 28 to 74, mean ± SD 56.7±10.16 years) and 68 (46.8%) females (age range of 29 to 74, mean ± SD 52.5±9.15 years) without statistical difference in their age distribution.

Their systolic blood pressure, diastolic blood pressure and mean arterial pressure ranged from 140 to 210, 72 to 148 and 60 to 135 respectively, and the mean (±standard deviation) was 165.3 (±15.7), 99.3 (±14.7) and 99 (±15.8) mm of Hg respectively.

Mean systolic blood pressure was more among females (167.26±15.77 mmHg) than males (163.57±15.51mmHg), similarly diastolic blood pressure

was also more among them (104.08±15.75) than their counterparts (95.27±11.37) thus identifying them to be a vulnerable population hitherto undetected. Hypertension was classified according to JNC VII, as stage I in 37 patients (25.2%) and stage II in 110 patients (74.8%). Isolated systolic hypertension was observed in 17 males and 6 females.

Microalbuminuria was seen in 51 cases (34.6%), and it was independent of age, sex, blood pressure status but it significantly correlated with retinal involvement (p=0.001), left ventricular mass (p=.034) and diastolic dysfunction (p=.014).

Overall retinal involvement was seen in 102 (72.1%). Retinal changes were significantly more in those with increased left ventricular mass and diastolic dysfunction.

The mean left ventricular mass was higher among males (264.85±71.79 gms) than females (231.59±74.86) and it was statistically significant. Left ventricular mass though increased with blood pressure, it was not significant statistically. At the same time left ventricular mass correlated with diastolic dysfunction, thus indicating that end organ damage has multiple factors viz., genetic susceptibility, endothelial damage, duration of blood pressure, subclinical stress.

Moreover the clinical symptom of giddiness was significantly more (p=0.015) among those patients with a higher left ventricular mass.

In view of the covert end organ damages viz., microalbuminuria, retinopathy, higher left ventricular mass and left ventricular dysfunction that were observed among newly detected non overweight, non smoking, non alcoholic, non dyslipidemic newly detected essential hypertensives of rural areas, there is an urgent need to design and implement “National Hypertension Detection and Control Programme” by the Ministry of Health and Family Welfare, Govt. of India with the help of professional medical associations and non governmental organizations. It is time to act, better late than never, in order to prevent or minimize hypertension induced complications.

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ANNEXURE I

Approval letter from the Ethical Committee

K. Dis.No. 27144/E4/1/2005.

Govt. Rajaji Hospital,
Madurai – 625 020. Dt. 06.04.06.

Sub: Establishment – Govt. Rajaji Hospital, Madurai – Ethical Committee Projects approved by the Committee – Intimation – Sent – Reg.

The Ethical Committee of the Govt. Rajaji Hospital, Madurai was held at 12 Noon on 01.04.2006 at the Dean's Chamber, Govt. Rajaji Hospital, Madurai, and the following Projects were approved unanimously by the Committee Members.

S.No.	Name of the Student	Name of the Project approved
01)	Dr.G.Madhusudhanan, CRRI,Govt. Rajaji Hospital.	Diabetic Foot Syndrome.
02)	Dr. G, Ramesh, PG in MD (Gen.Med.) Madurai Medical College.	Micro albumin Urea in HIV/AIDS patients.
03)	Dr. P. Thirumalaikolundu Subramanian, Professor & HOD of Medicine.	Autonomic Neuropathy among AIDS cases
04)	-do-	Lidovudine level in AIDS cases
05)	-do-	Lactic acid levels among AIDS cases
06)	-do-	Post Traumatic stress disorder among AIDS patients.
07)	-do-	Computer knowledge and lifestyle among HCWS
08)	Dr. D. Babu Vinish, PG in MD(Gen. Med.) Madurai Medical College.	Target organ damage in hypertension.
09)	Dr. K. Sidharthan, PG in MD.(Gen. Med.) Madurai Medical College.	Serum Sodium Potassium profile in hypertensives.
10)	Dr. Revathy Janakiraman, Addl.Prof.of Obst.& Gyn. Madurai Medical College.	Changing trends in Caesarean sections
11)	-do-	Awareness of contraceptives and HIV among unwed pregnant teenagers.
12)	Dr. V. Pavanasakumar, PG in MD(Gen. Medi.) Madurai Medical College.	Echocardiographic assessment of Cardiac dysfunction in patients of Chronic renal failure.
13)	Dr. M. Rajkumar, PG in MD (Gen.Med.) Madurai Medical College.	Optimal use of Anti-Snake venom in snake-bite envenomation.
14)	Dr.O.Chandran, PG in MD(Gen.Med.)	Socio demographic and Clinical aspects of acute diarrhoeal disease among adults.

S.No.	Name of the Student	Name of the Project approved
15)	Dr. P. Thirumalaikolundu Subramanian, Professor & HOD of Medicine, .	Injection practices among CRRIs.
16)	-do-	Specific learning disorders among HIV positive children.
17)	Dr. D. David Praveen Kumar, PG in MD(Gen.Med.)	Elderly Tuberculosis.
18)	Dr. Vipindas.C. PG in MD (Gen.Med.)	Music and Memory.
19)	Dr.M. Srinivasan, MBBS Student, Madurai Medical College.	Prevalance of Lipodystrophy among HIV/AIDS patients.
20)	Dr.E. Manivannan, PG in Pharmacology.	Cutaneous drug eruptions with special reference to non steroidal anti-inflammatory drugs.
21)	Dr. K. Baskaran, PG in Pharmacology.	Prescriptions and Doctors.
22)	Dr. S. Murugesan, PG in MD (Gen.Med.)	Congestive Cardiac failure.

Please note that the investigator should adhere the following:-

01) She/He should get a detailed informed consent from the patients/participants and maintain confidentially.
02) She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
03) She/He should inform the Institution Ethical Committee in case of any change of study procedure site and investigation or guide.
04) She/He should not deviate for the area of the work for which applied for Ethical clearance.
05) She/He should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
06) She/He should abide to the rules and regulations of the Institution.
07) She/He should complete the work within the specific period and apply for, if any extension of time is required, She/He should apply for permission again and do the work.
08) She/He should submit the summary of the work to the Ethical Committee on completion of the work.
09) She/He should not claim any funds from the Institution while doing the work or on completion.
10) She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

Dean/Chairman,
Ethical Committee, Govt. Rajaji Hospital, Madurai.

ANNEXURE II

PROFORMA

TOD AMONG NEWLY DETECTED RURAL HYPERTENSIVES

Name: OP No.: Age: Sex:

Sl. No.		**General examination**		**Investigations**	
Complaints		Anaemia		Blood sugar	
Giddiness		Jaundice		Urea	
Palpitation		Cyanosis		Sr. Creatinine	
Dyspnoea		Clubbing		Sr. Cholesterol	
Chest discomfort		LNE			
Headache		Pedal oedema		**ECG**	
Vertigo		Pulse rate /min		HR	
Weakness		BP Rt UL – mmHg		PR	
Swelling of legs		**CVS**		QRS QT	
Others		Apical Impulse			
Personal History		JVP		AXIS	
Smoker		Pericardium Pulsations		ST – T Segment	
Alcoholic		Epigastric pulsations		Q Waves	
Family History		S1			
DM		S2			
HT		Added sounds		Income	
CAD		Murmur		Education	
Past History		**RS**		Weight	
DM		Breath Sounds		Height	
TIA		Added Sounds		BMI	
CVA		**CNS**			

ECHO CARDIOGRAPHY

a. Diastolic function indices

1. Mitral E Mitral A Mitral E/A

2. IVRT

3. Deceleration Time (DT)

b. Systolic function indices

Ejection Fraction %

c. Left Ventricular Mass

d. Valves

Retinopathy

Microalbuminuria

ANNEXURE - III

MASTER CHART

SL NO	SEX	AGE	BP(SYS)	BP(DIA)	JNC	RETINA	ALBUMIN	IVRT	DT	MITRAL E/A	LV MASS	RV6+SV1
1	1	60	174	72	2	1	5.0	2	2	0.67	332	15
2	1	45	156	90	1	0	19.0	1	1	1.14	115	23
3	2	30	170	140	2	0	72.0	1	1	1.09	205	12
4	1	64	200	100	2	1	23	1	1	0.83	242	37
5	1	40	150	90	1	3	30	2	2	0.67	361	42
6	1	46	140	118	2	1	5.0	1	1	0.58	306	38
7	2	37	150	86	1	0	5.0	1	1	1.2	234	36
8	1	56	150	104	2	1	20.0	1	1	1.3	179	15
9	1	56	170	80	2	1	7.0	1	1	2.2	200	30
10	1	70	190	90	2	0	20.0	1	1	0.67	170	22
11	2	42	188	110	2	0	5.0	1	1	1.3	147	24
12	2	50	190	110	2	1	18.0	1	1	1.2	209	30
13	1	40	140	92	1	0	6.0	2	2	1.5	187	23
14	2	50	140	120	2	1	200	2	2	0.27	383	23
15	1	40	160	110	2	1	18	2	1	2.8	298	37
16	1	65	150	90	1	2	94	1	1	1.7	154	15
17	2	67	180	120	2	2	42	1	1	2	83	13
18	1	60	200	130	2	2	50	2	2	0.66	143	13
19	1	70	170	110	2	2	2	2	2	0.75	400	38
20	1	60	160	92	2	1	2	2	2	0.8	340	8
21	2	53	170	108	2	0	5.0	1	1	1.4	111	27
22	2	56	176	106	2	0	27	1	1	1.3	162	14
23	1	74	142	92	1	0	20	2	2	0.8	290	25
24	1	52	164	108	2	1	8	2	2	0.8	274	26
25	2	50	182	132	2	0	7.0	1	1	1.4	214	18
26	2	50	176	96	2	0	5.0	1	1	1.05	152	19
27	2	70	188	102	2	2	13.0	2	2	0.8	249	23
28	1	70	170	72	2	1	5.0	2	2	0.88	274	38
29	2	57	140	90	1	0	5.0	1	1	1.25	150	12
30	2	47	142	86	1	2	72.0	2	2	0.88	263	16
31	2	65	168	90	2	2	9.0	2	2	0.625	267	36
32	2	45	180	100	2	0	12	1	1	1.12	123	24

SL NO	SEX	AGE	BP(SYS)	BP(DIA)	JNC	RETINA	ALBUMIN	IVRT	DT	MITRAL E/A	LV MASS	RV6+SV1
33	1	48	150	90	1	1	72.00	2	1	1.3	214	19
34	2	55	210	112	2	1	18.5	2	2	0.7	285	26
35	1	67	162	88	2	0	7.0	2	2	0.8	313	22
36	1	74	162	72	2	0	5.0	1	1	2.4	192	30
37	1	49	158	102	2	1	12	2	2	0.54	409	25
38	2	49	156	110	2	2	21.0	2	1	1.16	203	13
39	2	50	188	146	2	1	100	2	2	0.75	309	14
40	2	48	168	102	2	2	112	1	1	0.8	180	14
41	1	65	180	80	2	0	72.00	2	2	0.71	190	18
42	2	61	172	100	2	2	39	1	1	0.75	206	18
43	2	55	150	100	1	2	74	1	1	0.6	229	20
44	2	41	168	94	2	0	9.0	1	1	1.65	120	28
45	2	50	160	100	2	1	19	1	1	1.4	147	20
46	2	50	162	108	2	0	5.0	1	1	1.6	195	20
47	1	40	140	100	2	1	12	2	2	0.9	308	25
48	2	60	180	90	2	1	72.00	2	2	0.2	265	25
49	2	47	152	98	1	0	5.0	2	2	0.2	264	15
50	1	70	148	88	1	1	5.0	2	2	2.72	272	19
51	2	65	150	90	1	2	5.0	2	2	0.27	279	38
52	2	55	162	88	2	1	134	2	2	0.6	401	16
53	2	57	180	130	2	1	7	2	2	0.23	340	15
54	2	60	148	92	1	0	9	1	1	2.5	230	17
55	2	29	176	132	2	2	24	2	2	2.81	251	32
56	2	45	176	98	2	2	36	2	2	0.87	350	24
57	2	62	158	102	2	1	15	2	1	0.75	287	11
58	2	35	174	126	2	2	32	2	1	1.5	278	38
59	2	45	150	92	1	1	5	1	1	0.73	374	16
60	1	67	160	90	2	1	18	2	2	0.94	290	39
61	1	56	168	104	2	0	8	2	2	0.64	282	17
62	1	60	192	98	2	3	29	2	2	0.81	349	20
63	1	58	156	96	1	1	5.0	2	2	0.6	287	20
64	1	54	184	90	2	1	29	2	2	0.73	285	28
65	1	28	152	102	2	2	72.00	2	2	0.6	319	36
66	1	51	178	90	2	2	5.0	2	2	0.6	326	25
67	1	54	178	94	2	2	20	2	2	0.75	274	38

SL NO	SEX	AGE	BP(SYS)	BP(DIA)	JNC	RETINA	ALBUMIN	IVRT	DT	MITRAL E/A	LV MASS	RV6+SV1
68	1	44	182	98	2	1	32	2	2	0.75	405	40
69	2	48	158	92	1	0	18	1	1	1.33	250	30
70	2	37	148	92	1	0	16	1	1	1.64	102	18
71	1	54	148	98	1	0	6.0	1	1	0.69	201	11
72	2	56	146	100	2	1	18.0	1	1	1.14	189	14
73	1	48	162	94	2	1	14.0	2	2	2.81	291	34
74	1	52	158	100	2	2	13.0	1	1	0.83	286	18
75	1	63	152	92	1	0	9	1	1	1.09	226	17
76	2	52	152	96	1	1	5.0	1	1	1.2	116	13
77	1	68	162	90	2	1	5.0	1	1	0.59	283	24
78	1	55	180	110	2	2	102	2	2	0.67	318	36
79	2	59	176	104	2	2	7200	2	2	0.54	296	39
80	1	51	146	96	1	0	8	1	1	1.3	242	14
81	1	65	178	76	2	1	6	2	2	0.37	320	36
82	2	50	160	90	2	0	7	1	1	1.5	215	20
83	2	50	172	100	2	1	13	1	1	1.2	240	25
84	1	54	150	92	1	1	5.0	1	1	1.3	250	26
85	1	46	148	92	1	0	14.0	1	1	1.4	156	12
86	2	47	160	100	2	1	6	1	1	0.92	260	25
87	1	50	150	86	1	0	8	1	1	1.7	240	25
88	1	66	160	104	2	2	152	2	2	0.6	313	14
89	2	48	152	90	2	1	14	1	1	1.5	215	28
90	1	45	170	100	2	2	56	2	2	0.86	286	16
91	1	44	142	116	2	1	12.0	1	1	0.9	214	39
92	2	40	154	90	1	0	5.0	1	1	1.4	232	22
93	1	60	150	100	2	1	9.0	1	1	1.3	180	16
94	1	62	174	84	2	1	14	1	1	1.4	222	32
95	2	72	200	100	2	2	48	2	2	0.9	291	38
96	2	45	172	100	2	0	16	1	1	1.8	150	24
97	1	54	188	108	2	1	12	1	1	1.9	200	30
98	1	35	142	96	1	0	10	2	2	1.62	186	22
99	2	54	146	116	2	1	24	2	2	0.6215	380	25
100	1	55	162	112	2	1	13	2	1	0.81	300	38
101	1	66	152	88	1	2	21	1	1	1.8	155	16
102	2	68	182	116	2	2	22	2	1	1.7	183	15

SL NO	SEX	AGE	BP(SYS)	BP(DIA)	JNC	RETINA	ALBUMIN	IVRT	DT	MITRAL E/A	LV MASS	RV6+SV1
103	1	62	198	130	2	2	82	2	2	0.84	299	38
104	1	72	168	108	2	2	200	2	2	0.53	400	39
105	1	62	164	90	2	1	126	2	2	0.76	340	10
106	2	55	172	110	2	0	12	1	1	1.9	110	28
107	2	60	162	94	2	0	8	1	1	1.4	162	24
108	1	62	178	100	2	1	23	1	1	1.8	164	16
109	1	74	144	90	1	0	19	2	2	0.82	288	25
110	1	54	166	100	2	1	16	2	2	0.96	276	24
111	2	54	180	130	2	1	7	1	1	1.9	220	20
112	2	54	174	92	2	0	5.0	1	1	2.4	154	20
113	1	68	186	100	2	2	19.0	2	2	0.91	268	25
114	2	74	172	72	2	1	14.0	2	2	24.0	280	38
115	1	56	142	90	1	0	9	1	1	0.78	152	13
116	2	50	144	86	1	2	32	2	2	24.0	260	17
117	2	66	166	90	2	2	14	2	2	26.01	268	37
118	1	46	170	100	2	1	8	1	1	17	125	25
119	1	50	152	88	1	1	2	2	1	16	215	20
120	2	56	208	110	2	1	2	2	2	35.0	286	27
121	1	68	160	90	2	0	14	2	2	0.84	312	28
122	1	74	164	74	2	0	7	1	1	1.93	194	32
123	1	50	160	100	2	1	6	2	2	0.59	408	38
124	2	52	158	112	2	2	2	2	2	0.88	248	15
125	2	54	180	142	2	1	42	2	2	0.94	310	16
126	1	74	164	74	2	0	7	1	1	1.82	194	28
127	1	52	156	102	2	1	12	2	2	0.78	400	27
128	2	51	158	110	2	2	29	2	1	1.43	206	16
129	2	52	186	148	2	1	112	2	2	0.92	311	18
130	2	54	166	100	2	2	52	1	1	0.85	278	38
131	1	52	176	90	2	2	19.0	2	2	0.87	327	36
132	1	60	176	94	2	2	18.0	2	2	0.97	276	38
133	1	52	180	88	2	1	34	2	2	0.94	286	29
134	1	54	154	96	1	1	18	2	2	0.83	288	20
135	1	60	194	98	2	3	200	2	2	0.79	350	21
136	1	64	182	80	2	1	11	2	2	1.9	194	20
137	2	64	176	100	2	2	14	1	1	0.93	208	20

SL NO	SEX	AGE	BP(SYS)	BP(DIA)	JNC	RETINA	ALBUMIN	IVRT	DT	MITRAL E/A	LV MASS	RV6+SV1
138	2	57	152	100	1	2	28	1	1	0.98	213	22
139	2	43	166	92	2	0	11	1	1	1.7	122	13
140	1	52	162	98	2	1	9	1	1	1.68	230	20
141	2	52	164	110	2	0	5.0	1	1	1.4	196	22
142	1	42	142	102	2	1	14.0	2	2	0.83	310	26
143	2	62	182	88	2	1	38	2	2	0.89	286	26
144	2	50	150	100	1	0	3	2	2	0.94	366	16
145	1	68	150	88	1	1	19.0	2	2	0.78	284	19
146	1	57	166	102	2	0	14	2	2	0.93	284	17
147	1	54	158	98	1	0	11	1	1	1.9	210	12

SL NO	EF	EDU	INCOME	HEALTH SEEKING BEHAVIOUR	GIDDINESS	BREATHLESSNESS	CHEST PAIN	HEADACHE
1	1	12	5000	1	0	1	0	0
2	1	0	2000	1	0	0	0	0
3	1	12	3000	1	1	0	0	0
4	1	0	1000	1	0	0	0	0
5	1	5	1500	1	0	0	0	1
6	1	5	1500	2	1	0	0	1
7	1	5	1300	1	1	0	1	1
8	1	1	800	1	0	1	0	0
9	1	6	1000	1	1	0	0	0
10	1	4	1000	1	0	0	0	0
11	1	7	1500	1	1	0	0	0
12	1	0	600	1	0	1	1	0
13	1	10	1300	1	1	0	0	0
14	1	0	1000	2	1	0	0	0
15	1	0	600	1	1	1	1	0
16	1	6	1600	1	0	0	0	0
17	1	0	600	1	1	0	0	0
18	1	0	600	2	1	0	0	0
19	1	0	500	1	1	0	0	0
20	1	3	5000	1	1	0	1	0
21	1	5	2600	1	1	0	0	0
22	1	3	3000	1	1	0	0	1
23	1	0	1800	1	1	0	0	0
24	1	0	3000	2	0	1	0	0
25	1	8	3000	1	1	0	0	0
26	1	0	1000	1	1	0	0	1
27	1	3	750	1	0	0	1	0
28	1	0	1500	1	1	0	1	0
29	1	5	800	1	1	1	1	1
30	1	5	1500	1	0	1	1	0
31	1	0	1500	1	0	0	1	0
32	1	3	600	1	1	1	1	0

SL NO	EF	EDU	INCOME	HEALTH SEEKING BEHAVIOUR	GIDDINESS	BREATHLESSNESS	CHEST PAIN	HEADACHE
33	1	12	9900	1	0	0	1	1
34	1	5	4000	2	0	0	0	1
35	1	2	600	1	0	0	0	0
36	1	7	1000	1	0	0	0	0
37	1	5	600	1	0	0	0	0
38	1	0	600	1	1	0	0	1
39	1	0	1000	1	1	0	0	1
40	1	0	1000	1	0	0	0	0
41	1	0	600	1	0	0	0	0
42	1	5	900	1	0	0	0	0
43	1	0	3000	1	0	1	0	0
44	1	5	1000	1	1	1	0	0
45	1	0	2000	1	0	0	0	1
46	1	5	2000	1	0	1	0	0
47	1	8	2000	1	1	0	1	0
48	1	4	4000	1	1	0	0	0
49	1	0	800	1	1	0	0	0
50	1	5	1200	2	0	0	1	0
51	1	0	500	1	0	0	1	0
52	1	9	1800	1	1	0	0	0
53	1	5	1500	1	1	0	0	0
54	1	4	900	1	1	1	1	0
55	1	3	600	1	1	0	0	0
56	1	0	2000	1	0	0	1	0
57	1	5	1000	1	0	0	1	0
58	1	15	2000	1	0	1	0	0
59	1	0	1500	1	1	0	1	0
60	1	8	1200	1	1	0	0	0
61	1	6	2000	1	0	1	0	0
62	1	7	2000	1	1	0	0	0
63	1	3	1000	1	1	0	0	0
64	1	8	1000	1	1	0	0	0
65	1	9	3000	1	1	0	0	0
66	1	5	700	1	1	0	0	0
67	1	8	2225	1	0	0	0	0

SL NO	EF	EDU	INCOME	HEALTH SEEKING BEHAVIOUR	GIDDINESS	BREATHLESSNESS	CHEST PAIN	HEADACHE
68	1	6	1000	1	0	1	1	0
69	1	12	2400	2	1	0	1	0
70	1	8	1200	1	0	0	0	1
71	1	10	2800	1	1	0	0	0
72	1	3	800	1	0	0	0	1
73	1	5	3000	1	0	0	0	0
74	1	2	1500	1	0	1	0	0
75	1	0	900	2	0	0	1	1
76	1	0	800	1	0	1	0	0
77	1	3	800	1	0	1	1	0
78	1	5	6000	1	1	0	1	0
79	1	4	900	1	1	0	0	1
80	1	9	2600	1	1	1	0	1
81	1	4	5000	1	1	0	1	0
82	1	10	2000	1	1	0	0	1
83	1	5	1500	1	1	1	0	0
84	1	8	3000	1	0	0	0	0
85	1	11	3200	1	0	0	0	1
86	1	8	1000	1	1	0	0	0
87	1	10	2000	1	1	0	0	0
88	1	0	800	2	0	0	1	0
89	1	7	1500	1	1	1	0	0
90	1	5	1000	1	0	0	0	0
91	1	6	1600	2	0	1	0	0
92	1	4	600	1	0	0	1	1
93	1	8	2000	1	1	0	1	0
94	1	3	600	1	1	1	0	0
95	1	0	500	1	1	1	1	1
96	1	5	1500	1	1	0	0	1
97	1	2	600	1	0	1	1	0
98	1	10	1600	1	1	0	0	0
99	52	2	600	1	1	1	1	0
100	1	4	1000	1	1	1	0	0
101	1	5	1000	1	0	0	0	0
102	1	0	600	1	1	0	0	1

SL NO	EF	EDU	INCOME	HEALTH SEEKING BEHAVIOUR	GIDDINESS	BREATHLESSNESS	CHEST PAIN	HEADACHE
103	1	2	600	2	1	1	1	0
104	1	6	800	1	1	0	0	1
105	1	3	800	1	1	0	1	1
106	1	6	2000	1	1	0	0	0
107	1	0	1800	1	0	0	1	0
108	1	4	2600	1	0	1	1	0
109	1	0	1600	1	1	0	0	0
110	1	2	800	2	0	1	0	0
111	1	9	3000	1	1	0	1	0
112	1	6	1000	1	1	0	0	1
113	1	3	850	1	0	0	1	0
114	1	7	1200	1	1	0	1	0
115	1	5	750	1	1	1	1	1
116	1	4	1300	1	0	1	1	0
117	1	0	800	1	0	0	1	0
118	1	3	600	1	1	1	1	0
119	1	11	8000	1	0	0	1	1
120	1	2	1750	2	1	0	0	1
121	1	2	600	1	0	0	0	0
122	1	0	450	1	0	0	1	0
123	1	3	600	1	1	1	0	0
124	1	0	600	1	1	1	0	1
125	1	2	300	1	1	1	1	1
126	1	6	1000	1	0	0	0	0
127	1	4	650	1	1	1	0	1
128	1	0	1450	1	1	1	0	0
129	1	2	1500	1	1	1	0	0
130	1	3	1250	1	1	0	1	0
131	1	5	850	1	0	0	0	0
132	1	8	2200	1	1	0	1	0
133	1	8	2000	1	1	0	0	0
134	1	3	1000	1	1	1	0	0
135	1	6	1500	1	1	0	0	0
136	1	1	500	1	0	1	1	0
137	1	5	900	1	1	0	0	1

SL NO	EF	EDU	INCOME	HEALTH SEEKING BEHAVIOUR	GIDDINESS	BREATHLESSNESS	CHEST PAIN	HEADACHE
138	1	2	2000	1	0	1	1	0
139	1	5	1200	1	1	1	0	1
140	1	1	600	1	0	0	0	1
141	1	5	1800	1	0	1	0	0
142	1	8	2600	1	1	0	1	0
143	1	4	600	1	1	0	0	0
144	1	0	800	1	1	1	0	0
145	1	5	1300	2	0	0	1	0
146	1	7	2200	1	0	1	0	0
147	1	8	3100	1	0	0	0	1

BP (SYS) - Blood Pressure (Systolic) BP (DIA) - Blood Pressure (Diastolic)

JNC - Joint National Committee VII Classification
Giddi - Giddiness
Breath - Breathlessness
Chest - Chest discomfort
Head - Headache

EF- Ejection Fraction
Edu - Education
HSB - Health Seeking behaviour

1- Male
2 - Female

IVRT
1- Normal
2- Abnormal

DT
1- Normal
2- Abnormal

HSB
1- Allopathy
2- Native Medicine

Symptomology
0-No symptom
1- Presence of symptom

Table 13: Age and Gender based classification of Retinopathy

No. of Patients			Retinopathy Grade	Age Group (in years)					
				<45		45-65		>65	
Male	Female	Total		Male	Female	Male	Female	Male	Female
21 (46.7%)	24 (53.3%)	45 (30.6%)	0	3 (27.3%)	9 (69.2%)	9 (19.1%)	15 (31.9%)	9 (42.9%)	0
39 (63.9%)	22 (36.1%)	61 (41.5%)	I	5 (45.5%)	1 (7.7%)	28 (59.6%)	20 (42.6%)	6 (28.6%)	1 (12.5%)
19 (46.3%)	22 (53.7%)	41 (27.9%)	II & III	3 (27.3%)	2 (13.63%)	10 (21.3%)	12 (54.55%)	6 (28.6%)	7 (31.82%)

In the age group part of the table the percentage is divided in such a way that the total of all males and female are made upto 100%.

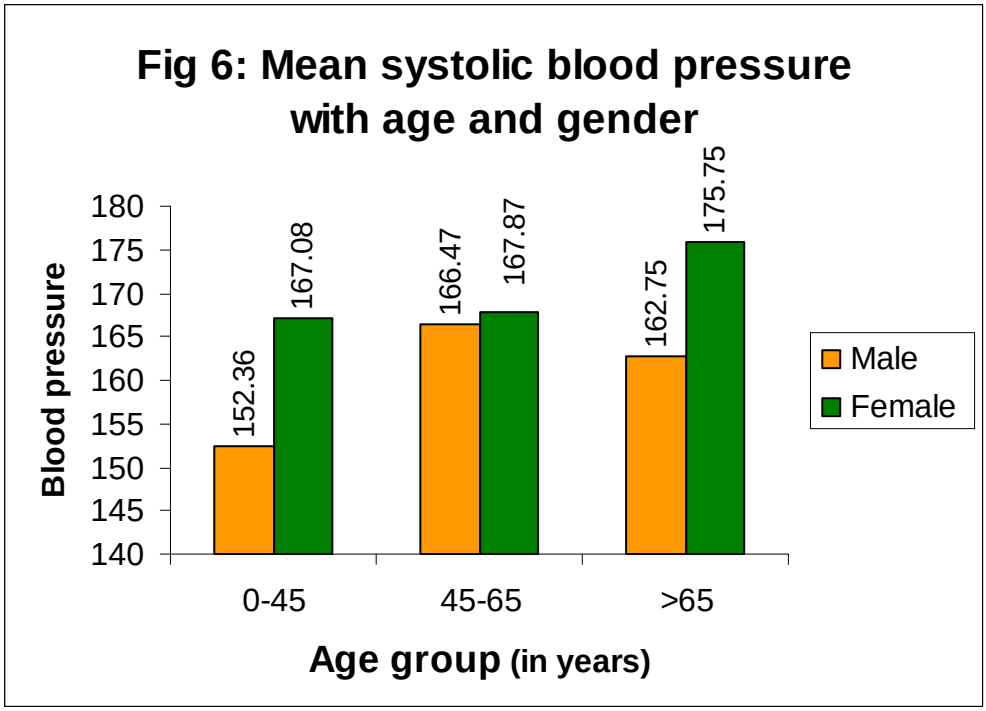
Fig 6: Mean systolic blood pressure with age and gender
Blood pressure
180
175
170
165
160
155
150
145
140
152.36
167.08
166.47
167.87
162.75
175.75
0-45
45-65
>65
Age group (in years)
Male
Female

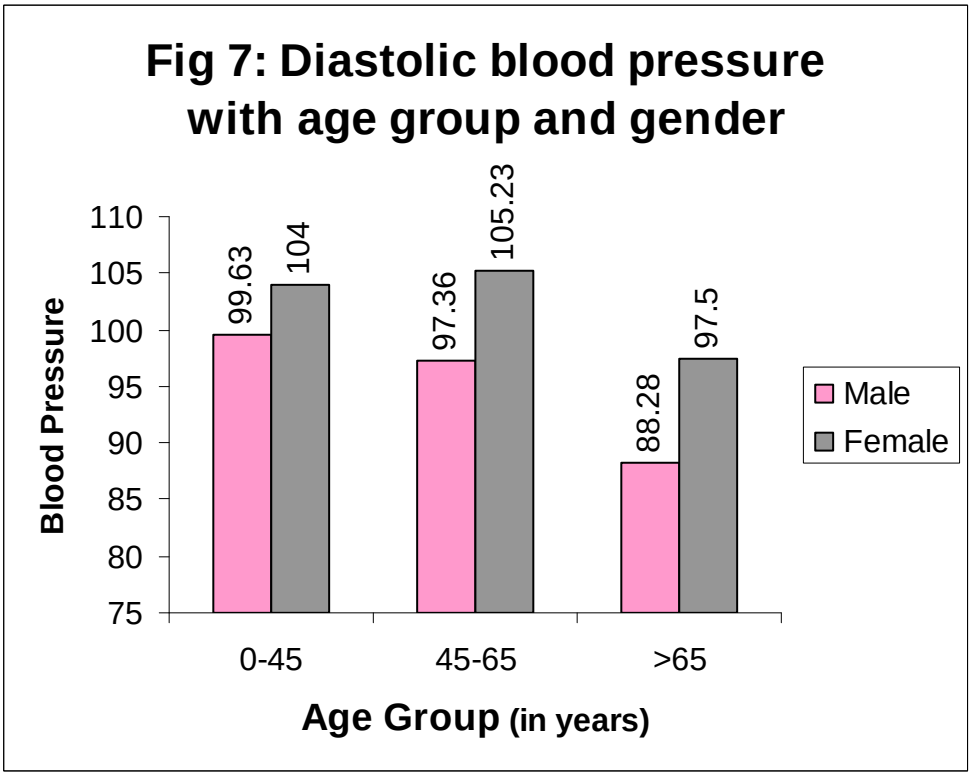
Fig 7: Diastolic blood pressure with age group and gender
Blood Pressure
110
105
100
95
90
85
80
75
99.63
104
97.36
105.23
88.28
97.5
0-45
45-65
>65
Age Group (in years)
Male
Female

Fig 8: Categorization of Patients as per age and gender according to JNC VII

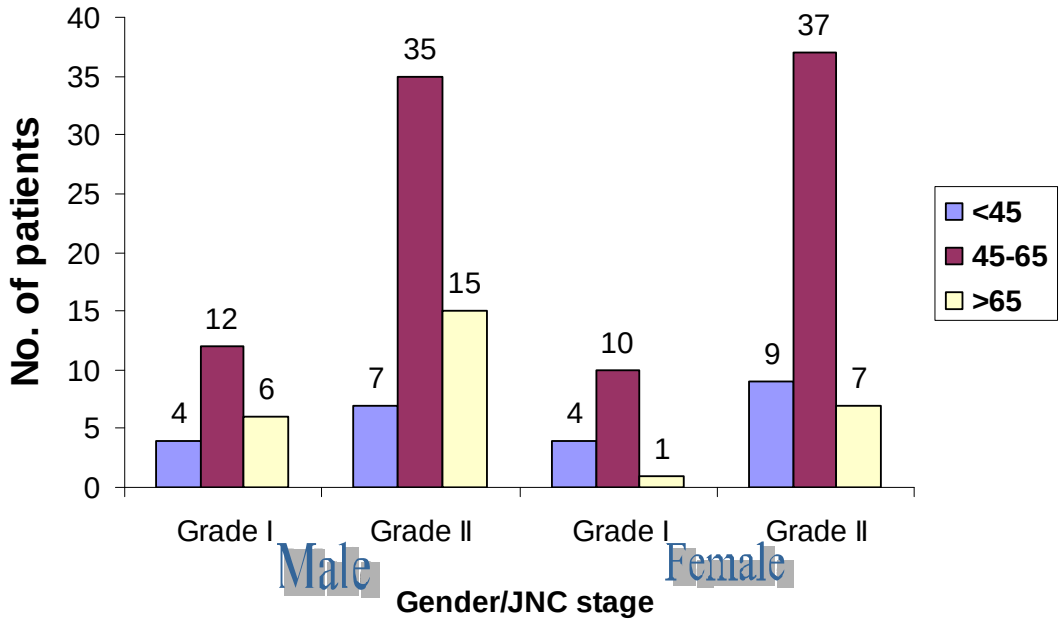

Fig 9: Pattern of Retinal involvement in patients with microalbuminuria

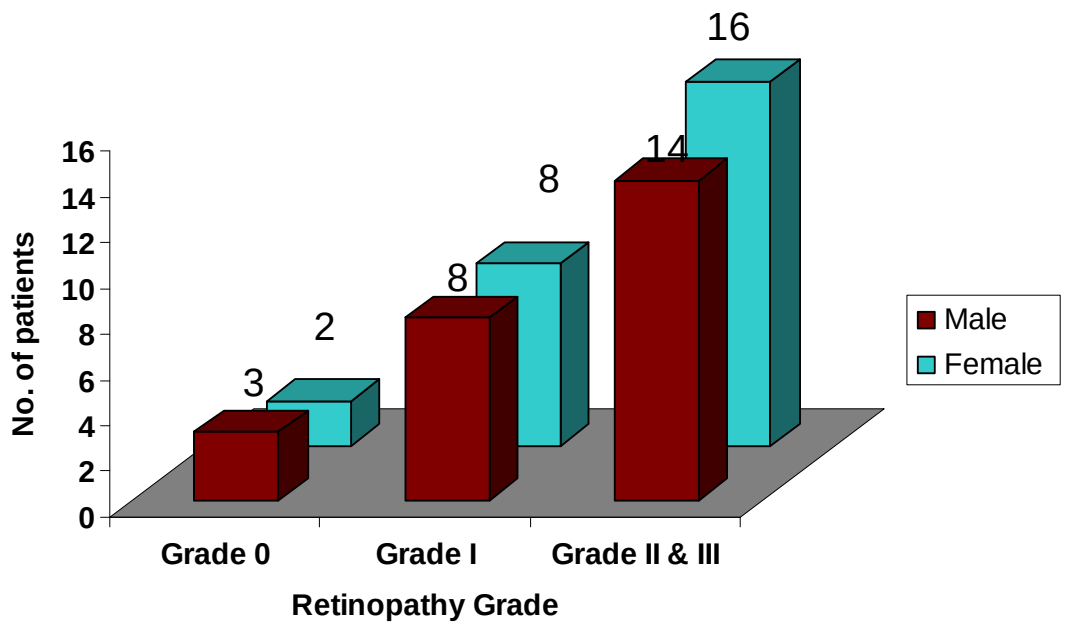

Fig 10: Pattern of Target organ damage in the Male study population

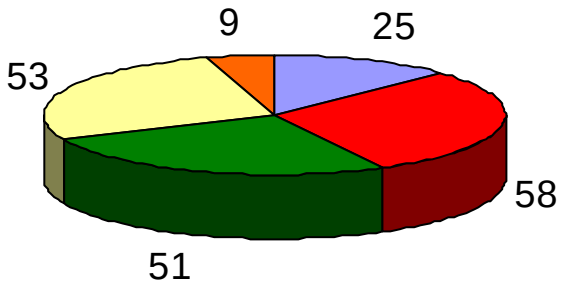

Fig 11: Pattern of Target organ damage in the Female study population